BIOMEDICAL ENGINEERING AND INSTRUMENTATION BRANCH

DIVISION OF RESEARCH SERVICES

NATIONAL INSTITUTES OF HEALTH

ANNUAL REPORT FY 1981

Dr. Murray Eden, Chief

Optimal [illegible] of Health (U.S.) Division of [illegible] Services. Biomedical Engineering and Instrumentation Branch.
Annual report fiscal year.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10001-13 BEI

PERIOD COVERED
October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)
Pharmacokinetics

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	R.L. Dedrick	Chief	ChES BEIB DRS
	J.M. Collins	Chemical Engineer	BEIB DRS
OTHER:	D.S. Zaharko	Pharmacologist	LCHPH NCI
	F. King	Associate Professor	Howard Univ.
	R.J. Lutz	Chemical Engineer	BEIB DRS
	P.M. Bungay	Chemical Engineer	BEIB DRS
	H.B. Matthews	Pharmacologist	NTP NIEHS
	I.G. Sipes	Assistant Professor	Univ. of Arizona
	C.E. Myers	Oncologist	CPB NCI
	M.F. Flessner	Chemical Engineer	US Coast Guard
	N. Bachur	Chief	LCB NCI
	J. Strong	Chemist	LCHPH NCI
	B. Smith	Neurosurgeon	SNB NINCDS

COOPERATING UNITS (if any)
LCHPH-NCI; LCB-NCI; SNB-NINCDS; CRD Program NIAMDD; M-NCI; NTP-NIEHS; CPB-NCI

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Chemical Engineering

INSTITUTE AND LOCATION
DRS, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
4.0	3.0	1.0

CHECK APPROPRIATE BOX(ES)

x(a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Pharmacokinetic models are developed for the distribution and disposition of drugs, environmental contaminants, and endogenous metabolites in animals and man. They provide a plausible set of equations that can be used to extrapolate data from animals to man and thereby improve chemotherapy, hemodialysis, and risk assessment.

Objectives: Improve and extend mathematical models for the distribution and disposition of drugs, environmental contaminants, and endogenous metabolites in animals and man to:

(1) Account for species differences in drug distribution.

(2) Provide a rational basis for extrapolating toxicity from animals to man.

(3) In conjunction with pharmacodynamics, provide a basis for optimizing cancer chemotherapy and chronic hemodialysis.

(4) Enable rational transfer of in vitro thermodynamic and kinetic data to in vivo cases.

(5) Predict effective dose schedules of anticancer drugs in individual patients with particular emphasis on intraperitoneal drug administration.

Methods Employed: Mathematical models are developed from physicochemical, physiological, and anatomical information and the principles of chemical reaction engineering. Resulting sets of differential equations are solved analytically or numerically and compared with experimental data. Uncertainties are clarified by additional experiments and model modification.

Major Findings:

(1) The rate of disappearance of 5-fluorouracil from peritoneal fluid in the rat has been experimentally measured and mathematically modeled. The rate of disappearance was about 10X higher at 24 M than at 12mM. A distributed model has been formulated which incorporates concepts of diffusion with saturable metabolism and nonsaturable capillary uptake in the tissue surrounding the peritoneal fluid. At high concentration, the model suggests that uptake by blood dominates the rate. At low concentrations (linear metabolism), metabolism dominates since it is about 80X faster than blood flow removal. This model also predicts that the effective penetration depth into tissue is highly dependent upon concentration.

(2) A theoretical analysis of the role of the lung in pharmacokinetics has been completed. This work was stimulated by several recent collaborations involving drugs with very large total body clearance. The analysis emphasizes the role of the lung in relation to its anatomic position. Several examples have been developed which demonstrate that a relatively small amount of pulmonary activity can have a large impact.

(3) The pharmacokinetics of the radiation sensitizers misonidazole and desmethylmisonidazole in the perfused rat liver have been modeled. Kinetic data from in-vitro experiments have been incorporated into the model to successfully predict the rate of formation of desmethylmisonidazole from misonidazole in the perfused liver system.

(4) Drug entry into the central nervous system in generally restricted by the blood brain barrier. The Ommaya reservoir provides a convenient means for obtaining serial samples of cerebrospinal fluid. Several recent studies of anticancer drugs have employed this device in either monkeys or humans. Pharmackinetic analysis of the results of these studies is on-going, and should provide the basis for extendingd our limited knowledge of CNS kinetics.

(5) A pharmacokinetic model is being developed for 5-methyltetrahydromofolate (MTHHF) in the mouse, rat, dog, and monkey. MTHHF inhibits the growth of a variant of L1210 leukemia which is resistant to folate antagonists and is entering clinical trial to study its effect against MTX-resistant solid tumors. MTHHF is not metabolized in any of the species and is excreted into the urine and feces. The model indicates that the free drug is cleared at GFR in all species. Both kidney clearance and biliary clearance vary with body weight to the 0.8 power.

(6) A physiologic model is being developed for the environmental contaminant tetrachlorodibenzofuran (TCDF) in mice, guinea pigs, rats, and monkeys. TCDF is a contaminant in PCBs and is present in incinerator fly ash and flue gases. TCDF toxicity is highly species dependent. Metabolized TCDF is readily cleared to urine and feces. The liver, fat, and skin are major depots of TCDF in the body. A PCB-type model with a combined excretion term has been used to model the drug in all species.

(7) A distributed mathematical model has been developed to describe transport of uncharged water soluble substances between plasma and peritoneal fluid. The model includes diffusion and convectrion through peritoneal tissue, lymphatic uptake, and transport across blood capillaries, which are assumed to be distributed uniformly in the tissue. The model has been applied to experimental data for the trasnport of substances ranging in molecular weight from 180 to 160,000 Daltons in the rat, and model parameters have been estimated.

Significance: Drugs and other chemicals are tested for effect in animals, with the aim of extrapolating results to man. At issue are both the risk associated with environmental contaminants and optimization of therapy.

Proposed Course: Continued pharmacokinetic modeling with consideration of pharmacodynamic and cytokinetic events and drug interactions. Continued clinical emphasis through support of intraperitoneal procedures and other measures to overcome drug resistance. Increased emphasis on research designed to investigate distribution and metabolism of environmental contaminants and on methods for incorporating pharmacokinetics in models of risk assessment. Investigation of use of in vitro assays of chemical metabolism in conjunction with pharmacokinetic models for quantitative prediction of metabolism in vivo.

Publications:

Lutz, R.J., Dedrick, R.L. and Zaharko, D.S.: pharmacokinetics: an in-vivo approach to membrane transport. Pharmacol. Therapeutics 11:559-592 (1980).

Reprinted in International Encyclopedia of pharmacology and Therapeutics, Membrane Transport of Chemotherapeutic Agents, I.D. Goldman (Ed.), Pergamon, New York (In Press).

Speyer, J.L., Sugarbaker, P.H., Collins, J.M., Dedrick, R.L., et al.: Portal levels of hepatic clearance of 5-fluorouracil after intraperitoneal administration in man. Cancer Research 41:1916-1922 (1981)

Jones, R.B., Collins, J.M., MYers, C.E., et al.: High volume intraperitoneal chemotherapy with methotrexate in patients with cancer. Canc. Res. 41:55-59 (1981).

Collins, J.M. and Dedrick, R.L.: Contribution of the lung to total body clearance: linear and nonlinear effects. J. Pharm. Sci. (In Press).

Litterst, C.L., Collins, J.M., Lowe, M., et al.: Toxicity resulting from large volume intraperitoneal administrationof adriamycin in the rat. Cancer Treat. Rep.(In Press)

Monks, A., McManus, M.E., Collins, J.M., et al.: Non-linear pharmacokinetics of misonidazole in the perfused rat liver. Proc. Amer. Assoc. Cancer Res. (Abstract) 22:238 (1981).

King, F.G. and Dedrick, R.L.: Physiologic Model for the Pharmacokinetics of 2'deoxycoformycin in Normal and Leukemic Mice. J. Pharmacokin. and Biopharm. (In Press).

Collins, J.M. and Dedrick, R.L.: Pharmacokinetics of anticancer drugs. In Clinical Pharmacology of Antitumor Drugs, B.A. Chabner (Ed.), Saunders, Philadelphia (In Press).

Bungay, P.M., Dedrick, R.L., and Matthews, H.B.: Enteric Transport of Parent Chlordecone (Kepone®) in the Rat. J. Pharmacokin. Biopharm. (In Press).

Dedrick, R.L.: An Engineer's Perspective on Environmental Toxicology. 74th Annual AIChE Meeting. (In Press).

Dedrick, R.L.: Interspecies Dose-Response for Radiogenic Bone Cancer. Science (In Press).

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10002-16 BEI

PERIOD COVERED
October 1, 1980 to September 1981

TITLE OF PROJECT (80 characters or less)
Implant Device Development

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	J.W. Boretos	Physical Scientist	BEIB, DRS
OTHER:	W.S. Pierce	Associate Professor	Penn State University
	J. Doppman	Radiologist	CR, CC
	E. Glatstein	Chief	RO, NCI

COOPERATING UNITS (if any)
CR-CC; Pennsylvania Sate University, RO, NCI

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Chemical Engineering

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
2.0	1.7	0.3

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

The purpose of the project is to elucidate the interaction of biomaterials used for specific implants with the physiological environment and to explore specially prepared biomaterials and design features with respect to their suitability and performance in a variety of contexts. After removal from the host organism, implants will be examined for lipid absorption, changes in surface-free energy, and alteration of physical properties. Observations should include scanning electron microscopy, infrared spectroscopy, contact angle measurements, and energy dispersive X-ray analysis. Physical measurements will be made of tensile properties, flexural-fatigue resistance, electrical properties, hardness, density, coefficient of static and kinetic friction, hydrophilicity, and other surface and bulk properties.

Objectives: Elucidate the interaction of polymers, metals, and ceramics used for specific implants with the physiological environment; explore specially prepared polymers and design features with respect to their suitability and performance in a variety of contexts.

Methods Employed: Basic composition of biomaterials is carefully controlled, and modifications are employed to enhance acceptability by the living system. After removal, implants are examined for lipid absorption, protein and/or calcium deposition, changes in surface-free energy, and alteration of physical properties. Observation techniques include SEM, infrared spectroscopy, contact angle measurements, energy dispersive X-ray analysis, and atomic absorption spectroscopy. Flow characteristics and pressure gradients across heart valve implants are studied in vitro in a test apparatus. Electronic implants are examined periodically in vivo for changes in threshold levels, corrosion, and tissue activity. In vitro studies of the aforementioned are designed to accelerate fatigue testing and methods of improvement through heat treatment of the metal components undergoing stress. Surfaces of cathethers are modified using surface treatments of grafted polymers and copolymers to reduce drag through the blood vessels. These catheters are tested for burst strength, stiffness, tensile strength, and density. The basic composition is modified through compounding. Embolizing agents consisting of composites of polymers, ceramics, and metals are being devised for delivery through the catheter systems so as to block arteries and vessels in the treatment of lesions such as aneurysms and arteriovenous malformations.

Major Findings: Several hydrogel polymers can be applied to the surfaces of microcatheters to increase lubricity thereby minimizing resistance to movement through narrow and winding vessels.

Significance: Physiologically compatible polymers with enduring strength are needed for such applications as heart valves, heart-assist devices, vascular implants, indwelling catheters, and subcutaneous uses.

Proposed Course: Extend experimental studies to further characterize the surface and bulk properties of biomaterials and, more specifically, determine their interactions with blood and subcutaneous tissue to facilitate development of better surfical implants.

Publications:

Boretos, J.W.: Encapsulation Considerations for Acute/Long Term Durability of Electronic Implants. In M. Szycher and W.J. Robinson (Eds.) Synthetic Biomedical Polymers: Concepts and Practices. Technomics Publishing Co., Westport, Conn. 1980, pp. 187-200.

Boretos, J.W., Terek, R.M., Girton, M.E. and Doppman, J.L.: Cohesive and Frictional Reduction of Intra-arterial Microcatheters. Proceedings of the 33rd Annual Conference on Engineering in Medicine and Biology, Washington, DC, September 1980, p. 74.

Boretos, J.W., Dengler, W.C., Terek, R.M., Edwards, K.J., Jr., Wilkins, J.F., Girton, M.E. and Doppman, J.L.: Integral Balloon Catheter for Interventional Radiology. Proceedings of the 33rd Annual Conference on Engineering in Medicine and Biology, Washington, DC, September 1980, p. 159.

Goldstein, S.R., Jones, R.E., Sipe, J.J., Doppman, J.L. and Boretos, J.W.: A Miniature Toposcopic Catheter Suitable for Small Diameter Tortuous Blood Vessels. J. Biomed. Engr. 102:221 (1980).

Boretos, J.W.: Selection Criteria for Polymeric Implant Applications with Representative Modifications for Increased Acceptability. In Ghista, Reul and Rau (Eds.) Perspective in Biomechanics, Harwood Academic Publ., NY, 1981.

Boretos, J.W.: The Chemistry and Biocompatibility of Specific Polyurethane Systems for Medical Use. In D.F. Williams (Ed.), Biocompatibility of Clinical Implant Materials, CRC Press, (In Press).

Boretos, J.W. and Edwards, K.J., Jr.: Drug Delivery Through An Integral Microcatheter. Proceedings 16th Annual Meeting of association for the Advancement of Medical Instrumentation, Washington, DC, 1981, p. 17.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10007-07 BEI

PERIOD COVERED
October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)

Investigation of Oxidative Metabolism and Potassium Kinetics in the Cat Brain

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	W.H. Schuette	Chief	ACES BEIB DRS
OTHER:	B.A. Vern	Clinical Associate	CNB NINCDS
	W.C. Whitehouse	Electronics Technician	ADM CC
	N. Mutsuga	Visiting Fellow	CNB NINCDS

COOPERATING UNITS (if any)

CNB-NINCDS; AB-CC

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Applied Clinical Engineering

INSTITUTE AND LOCATION
DRS, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
3.0	2.0	1.0

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Oxidative metabolism, as indicated by the fluorescence of nicotinamide adenine dinucleotide (NADH) and oxygen consumption, was assessed to investigate potassium ion kinetics in the cat brain. Research was conducted to determine if the potassium clearance process is active or passive after activation of the cortex. Investigations were also conducted to determine the applicability of the NADH fluorescence technique to exposed myocardium. Active work on this project was completed before September 30, 1977; additional papers were published in 1979 and 1980. One paper was also published this year.

Methods Employed: The NADH fluorescence at 470 nM is excited by illumination with ultraviolet light at 360 nM obtained from a high pressure Hg arc lamp. To compensate for blood volume changes within the field of interest, we developed and used a television fluorometer employing fluorescein dye as a reference. The technique, initially used for study of cat brain, was also applied successfully to exposed myocardium.

A potassium-sensitive microelectrode system was employed for measuring both extracellular and intravenous potassium ion levels.

Direct cortical oxygen consumption measurements were made by cannulation of the sagittal sinus and monitoring the flow rate and hemoglobin saturation of the blood flowing out of the sinus. The calculated oxygen consumption is proportional to the arterial-venous oxygen concentration difference multiplied by the flow rate.

For the Q_{10} experiments, the exposed cat hippocampus temperature was either elevated or lowered by use of a controlled temperature stream of artificial spinal fluid which flowed over the surface of the hippocampus. Surface temperature was monitored by a small thermistor probe.

Major Findings: The NADH dynamics observed in the myocardium are similar to those observed in the cortex.

Blood volume in transiently ischemic myocardial tissue may increase due to relaxed muscle tone.

Fluorescein fluorescence was found to be an excellent indicator of myocardial perfusion.

Agreement was found between an analytical model for potassium clearance and experimentally determined potassium kinetics. This agreement provided further evidence of the active clearance process previously suggested by Q_{10} measurements and the slowing of potassium clearance during periods of hypotension.

Publications:

Vern, B.A., Schuette, W.H., and Whitehouse, W.C.: Effects of Brain Stem Stimulation on Cortical NADH Fluorescence, Blood Flow, and O_2 Consumption in the Cat. Experimental Neurology, 71:581-600, 1981.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER 10 Z01 RS 10015-06 BEI

PERIOD COVERED

October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)

Development of Miniature Catheter for Clinical Use

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	D. Shook	Mechanical Engineer	BEIB DRS
OTHER:	S.R. Goldstein	Chief	MES BEIB DRS
	J.L. Doppman	Chief	DR CC

COOPERATING UNITS (if any)

DR-CC

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Mechanical Engineering

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, MD 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
1.0	.8	.2

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES x (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

A miniature toposcopic catheter attached to the end of a 1-mm #5 French catheter has been developed for insertion in tortuous blood vessels as small as 1 mm in diameter and up to 30 cm long. Catheter tests in anesthetized dogs have been highly successful - the catheter is able to penetrate parts of the vascular system which are inaccessible by existing techniques. The apparatus has been redesigned to provide the reliability and convenience required for clinical use. The catheter will enable the delivery of embolizing agents or other therapeutic substances so that some procedures previously requiring surgery can be performed instead with catheters. Techniques of steering the catheter are being developed and efforts are in progress to allow aspiration of fluid from remote areas.

Objectives: Develop techniques and devices for inserting a miniature catheter into small tortuous vessels and steering it into selected branches.

Develop techniques and devices for delivering therapeutic materials into the catheterized vessel for clinical usage and to aspirate fluids from these locations.

Major Findings: An improved miniature topographic catheter capable of negotiating tortuous paths has been successfully tested in dogs and will soon be ready for clinical use.

Significance: Surgeons and radiologists have long sought techniques for catheterizing small diameter vessels separated from larger, easily catheterized vessels by long, narrow passages with numerous bifurcations. The capability would permit selective treatment of tumors, aneurysms, and other lesions with minimal danger to normal tissues. Delivery of embolizing agents and materials to stain tissue, as well as aspiration of fluid, are contemplated.

Proposed Course: Complete modifications of the previously developed system, perform dog tests and then use the system clinically. Develop techniques for aspirating fluids for diagnostic purposes. Develop steering techniques, test in animals, and incorporate into the existing system. Develop related devices and explore additional uses for the catheter.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10018-06 BEI

PERIOD COVERED
October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)

Particulate Hydrodynamics in Porous Membranes

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	P.M. Bungay	Chemical Engineer	BEIB DRS
	M.E. O'Neill	Reader Mathematics	Univ. Coll., London

COOPERATING UNITS (if any)

Department of Mathematics, University College, London

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Chemical Engineering

INSTITUTE AND LOCATION
DRS, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
0.2	0.2	

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Mathematical models are being developed to describe passive membrane transport through pores or intracellular gap junctions. The Taylor-Aris dispersion analysis is extended to treat combined Brownian motion and convection in a single pore. The solute particle dimension is assumed to be large compared to that of the solvent molecules and also appreciable in size compared to the lateral pore dimension. The latter condition implies strong "hindered diffusion" and related solute-membrane interaction effects. A key aspect of the analysis is a generalized Einstein relation for predicting axial and radial components of the diffusivity tensor from hydrodynamics solutions for resistance coefficients. Perturbation techniques are used to obtain asymptotic solutions to the hydrodynamic equations, and the method of moments is employed to analyze the solute continuity equation. Related hydrodynamic problems are also being considered, such as flow through constricted vessels.

Objectives: The objective of this project is to provide the basis for a rigorous, predictive continuum theory for passive transport phenomena in porous membranes, including such observations as "hindered diffusion". The development of solutions to hydrodynamic problems of interest in other areas of the biological and physical sciences is also considered.

Methods Employed: The essence of the approach to membrane transport is an extension of the Einstein continuum analysis for the Brownian motion of spherical molecules in dilute solutions. Einstein derived his predictive relation for the diffusion coefficient from the theoretical expression for the hydrodynamic resistance to translation of a rigid sphere through a homogenous viscous fluid of infinite extent. The continuum analysis for porous membranes begins with a single solute molecule in a single pore and assumes that the form of Einstein's relationship between the diffusion and resistance coefficients remains valid. However, the presence of the rigid pore wall, in general, increases the hydrodynamic resistance to translation and rotation of the solute relative to the fluid. The diffusivity is thereby decreased in magnitude until, in the limit, as the solute dimension becomes equal to the lateral pore dimension, the diffusion coefficient falls to zero. Where there is, in addition to diffusion, net movement of the fluid through the pore, the hydrodynamic interaction similarly affects the solute flux relative to the solvent flux. The project is concerned with deriving the requisite expressions for the resistance coefficients from hydrodynamic theory as well as developing analyses for diffusive and convective porous membrane transport.

The primary theoretical tools used in the hydrodynamic problems are regular and singular perturbation techniques (typically using the ratio of solute to pore dimensions as the asymptotic expansion parameter) and collocation techniques of the type developed by Weinbaum and Pfeffer.

The transport analysis has been approached using the Taylor-Aris type dispersion treatment and the method of moments for deriving expressions for the pertinent coefficients without directly solving the complete solute continuity equation (convective-diffusion equation).

Major Findings: We completed the derivation of expressions correct to the second order in the sphere-to-tube radius ratio for the pressure drop due to the presence of neutral spherical solutes in cylindrical pores. Numerical computations using these expressions is proceeding.

An analysis was begun for describing the axisymmetric settling of a toroidal particle inside a vertical fluid-filled tube.

Proposed Course: In addition to the models presently under study, it would be desirable to examine a situation in which the solute is a nonspherical body in order to determine how to handle partical orientation and rotational Brownian motion effects. An ellipsoidal solute would be the likely choice in terms of posing theoretically tractable problems. Another direction to pursue, which would greatly extend the range of applications for the theory, would be to incorporate into the present models nonhydrodynamic solute-membrane interactions such as electrostatic or London Van der Waals attractive/repulsive forces.

Significance: Channels (pores, slitlike gap junctions) represent one important type of transmembrane transport in biological systems. A rigorous conceptual and predictive framework for pore theory would be useful in clarifying relevant biological transport and would find wide applicability in engineering and physical science work pertaining to synthetic membranes.

Publications:

Bungay, P.M. and O'Neill, M.E.: The pressure drop along a tube due to an axisymmetric constriction. J. Colloid Interface Science 71(2): 216-236, 1979.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10027-05 BEI

PERIOD COVERED

October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)

Development of Whole-Body Hyperthermia Instrumentation and Control System

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	W.H. Schuette	Chief	ACES BEIB DRS
OTHER:	J. Bull	Senior Investigator	MC DCT NCI
	D. Lees	Staff Anesthesia	CC NIH
	R. Corsey	Electronic Engineer	BEIB DRS
	H. Tipton	Mechanical Engineer	BEIB DRS
	R. Smith	Nurse	MC DCT NCI

COOPERATING UNITS (if any)

MC-DCT-NCI; CC-NIH; MS-DCT-NIH

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Applied Clinical Engineering

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
3	2	1

CHECK APPROPRIATE BOX(ES)

☒ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Whole body hyperthermia is being studied at NIH as a possible means of treatment for cancer. This project includes development of an instrumentation and control system based on utilization of a Tektronix 31 programmable calculator, digital plotter, and interface for data acquisition. The esophageal temperature of the patient is regulated to 0.1°C accuracy by feedback control of the temperature of water circulating in a set of hyperthermia blankets. The NIH phase of this project was completed August 1980, however additional publications have been made.

Methods Employed: A Tektronix 31 programmable calculator is being used to acquire, record, and process data as well as to control water temperature of a set of hyperthermia blankets. The temperature of the water pumped through the blankets together with esophageal and rectal temperatures of the patient are processed by the calculator, which then develops temperature commands for the water temperature mixing valve. The mixing valve adds hot or cold water to the flow stream returning from the blankets as directed by the Tektronix digital interface unit so that heart rate, blood pressure, and temperature data could be processed by the system. The multiplexer module also provides commands from the calculator to the water mixing valve motor. Automatic cool-downs are programmed into the calculator in response to various out-of-limit conditions. The calculator functions in an interactive mode for entry of operational instructions.

Major Findings: The major finding from the use of the equipment is that it is possible to take the whole-body core temperature of patients to 42.0 $\pm$0.1^{o}C for four hours on a biweekly basis without major difficulty. The finding suggests that hyperthermia treatment for cancer is practical. Currently, the system is being employed in conjunction with chemotherapy at the Herman Hospital, Houston, Texas.

Publications:

Smith, R., Bull, J.M., Lees, D.E. and Schuette, W.H.: Whole Body Hyperthermia: Nursing Management and Intervention. Cancer Nursing, pp. 185-189, June 1980.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10034-04 BEI

PERIOD COVERED
October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)
Three-Dimensional Histological Reconstruction

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI: S.B. Leighton Mechanical Engineer BEIB DRS

COOPERATING UNITS (if any)
None

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Mechanical Engineering

INSTITUTE AND LOCATION
DRS, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
.5	.45	.05

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

A semi-automatic system for acquisition of three-dimensional structural information about histological material is being developed. The system should have significant speed and reliability advantages over present techniques using serial sections, although resolution may be limited. In brief, an embedded tissue block will be fixed relative to a scanning electron microscope imaging system, the surface of the block will be imaged and stored, and successive slices will be removed by a built-in microtome. Handling and registration of thin sections will thus be eliminated. Human and computer pattern recognition will transform the resulting set of images into a three-dimensional reconstruction.

Objectives: (1) To facilitate making schematic diagrams of neural networks. (2) To facilitate developmental studies of small organs and organisms. (3) To do three-dimensional reconstruction of biological structures.

Methods Employed: A miniature microtome has been designed to function within the vacuum chamber of a scanning electron microscope. The microtome is designed using flex hinges and a hydraulic drive for the knife and flex hinges and a combination pneumatic, lead screw, and piezolelectric drive for the specimen. The specimens are embedded in epon and the cut faces are coated with a thin layer of gold-palladium to prevent charging. The microtome is operated from outside the SEM by means of the hydraulic and pneumatic tubes passing through a vacuum feedthrough. The sections are removed with a small argon jet.

Major Findings: The microtome has been constructed and tested successfully within the SEM. Satisfactory images of squid fin nerves have been obtained. Resolution so far has been 600 Angstroms.

Significance: Neuroanatomists may be able to trace significant neural nets with sufficient ease to allow a statistically significant number of samples.Other biological studies may be materially aided.

Proposed Course: The system will be integrated with an existing computer for image processing for semi-automatic three-dimensional reconstructions. Improved embedding media will be tested to give an etched surface effect to improve resolution. An improved gold-ion deposition system will also be added.

Publications:

Leighton, S.B.: "A Miniature Microtome for Use Inside Scanning Electron Microscope", 1981 Advances in Bioengineering, ASME, NY, (In Press)

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10041-04 BEI

PERIOD COVERED
October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)
Flow Visualization Studies and Hemodynamic Events in Model Arteries

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	R.J. Lutz	Chemical Engineer	BEIB DRS
OTHER:	R.L. Dedrick	Chief	ChES BEIB DRS
	D.L. Fry	Chief	H IR OD

COOPERATING UNITS (if any)
OD - IR - NHLBI

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Chemical Engineering

INSTITUTE AND LOCATION
DRS, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
0.7	0.4	0.3

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

The appearance of atherosclerotic lesions at specific locations in the arterial tree has led many investigators to study the relevance of hemodynamic factors in atherogenesis. The purpose of this study is to investigate the patterns of flow in models of arterial geometry, to measure velocity profiles at several cross sections, and to seek correlations between fluid mechanic events and the development of atherosclerotic plaques. Various methods of flow visualization such as dye injection, neutrally buoyant microsphere tracers and laser illuminated light scattering particles are being used to study the flow patterns in arterial models as a function of various flow parameters such as Reynolds number, branch flow ratios, and pulsatility. Both still photography and high-speed cinematography record the flow phenomena. The electrochemical technique measures average mass transfer coefficients to the artery wall under conditions of steady and pulsatile flow.

Objectives: The objectives of this study are to visualize and record the various kinds of flow phenomena such as flow separation and secondary flow that may occur in complex flow channels that represent arterial geometry and to correlate the flow phenomena with the location of atherosclerotic plaques in experimental animals. The analysis will include a quantitative measure of the velocity profiles at various sites in the model arteries. In conjunction with these experiments, measurements will be made of the mass transfer coefficients to the walls of the model arteries under conditions of both steady and pulsatile flow.

Methods Employed: Several methods have already been shown to be useful for visualizing flow patterns in our model systems, and other methods can be tried. The electrochemical method of measuring mass transfer coefficients is being used in several model systems. The following flow visualization techniques are being used.

(1) Dye injection. At selected sites in the arterial model, small ports are drilled for insertion of #30 gauge hypodermic tubing, which is connected via PE 10 catheter tubing to a reservoir of colored dye. The end of the hypodermic tubing can be positioned at any radial location in the flow model and the dye slowly injected into the flow to mark the streamlines. The streamline patterns at several sites are then recorded using 35-mm still photography. Data obtained by dye injection into the flow indicate that the flow streamlines are skewed toward the side-arm branches exiting from the main (aortic) flow channel and that unusual patterns of backflow and secondary flow occur near the dorsal channel wall just opposite the branch orifices. These phenomena are governed by the fraction of the flow that exits out each daughter branch.

(2) Neutrally buoyant microspheres. This method employs a dilute suspension of 100- to 500-micron diameter polystyrene microspheres in a 20 to 25 percent glycerine/water solution, which serves as the test fluid in the flow model. The microspheres are dyed with a fluorescent dye and then illuminated with ultraviolet light making them clearly visible in the flow system. The path of the microspheres are photographed with high-speed cinematography as these neutrally buoyant particles move along with the fluid. In such a manner, the direction and velocity of fluid elements can be determined. This method gives an overall view of the flow patterns throughout the bulk of the fluid flow.

(3) Laser Doppler velocimetry. When light is scattered from a moving object, a stationary observer will see a change in the frequency of the scattered light (Doppler shift) proportional to the velocity of the object. This Doppler shift is used to measure the velocity of particles at various locations in the fluid. From the particle velocity, the fluid velocity is inferred. A laser is used as the light source because it is easily focused and coherent. This method allows us to determine, quantitatively, the velocity profiles at various positions in the arterial model. Numerous profiles have been recorded in both steady and sinusoidal flow at various flow rates.

By passing the thin collimated laser beam through a cylindrical lens, a source of plane illumination can be created which can be used to visualize a specific narrow cross section in the flow channel by observing its light scattering effect from small

particles that move with the fluid. This technique exhibits, in two dimensions, various flow patterns like stream lines and separation eddies.

Major Findings:

Wall Shear Rates: Wall shear rates were measured by the electrichemical technique in a two-branch model representing the celiac and superior mesenteric branches in the canine aorta. Shear patterns were similar to those found earlier in a canine aortic cast of this region. The shear rate in the celiac branch varied considerably just inside the branch entrance as celiac flow was varied. Flow separation was not detected in this branch. Shear patterns inside the celiac branch were not sensitive to flow rates in the adjacent mesenteric branch. Shear rates on the aortic side of the celiac flow divider lip (which starts the approach to the mesenteric divider) was nearly linearly related to celiac flow but insensitive to mesenteric flow. Dorsal shear rates were much lower than ventral shear rates.

Velocity Profiles: Velocity profiles were obtained in two diametrical planes, one in the plane of branches (sagittal), the other perpendicular to that plane (lateral). The entrance to the model has a fully developed parabolic profile, but the sagittal profiles became skewed toward the branch side of the model as one progressed further downstream near and beyond the branches. Skewness increased with increasing branch flow rate. Flow separation and flow reversals were seen with the profile measurements at the proper flow conditions. Pulsatile flow representing a cardiac waveform generated velocity profiles distinctly different from steady flow results. Pulse profiles were very blunt and only showed reverse flow phenomena when the total flow rate was negative.

Wall Mass Transfer: Wall mass transfer coefficients were measured using the electrochemical technique for steady, sinusoidal, and pulsatile flow. For steady flow, the mass transfer patterns throughout the artery were the same as the shear patterns calculated previously since these two phemonena are interrelated. Pulsatile flow enhanced mass transfer from 50% to 100% in regions which would normally exhibit flow separation under steady flow conditions. In other regions, the average mass transfer coefficient for pulsatile flow was similar to that for steady flow at the same average flow rate.

Significance: Elucidation of the role of hemodynamics on the onset and development of atherosclerotic plaques is fundamental in the study of vascular disease. Certain biological evidence suggest that areas of increased plaque formation may correlate with areas frequently exposed to disturbed flow, for example, flow spearation, or to relatively stable flow patterns that change direction and magnitude periodically throughout the day with varying metabolica and blood flow demands. This study should demonstrate various types of flow patterns that can occur in arterial systems as a function of changing flow parameters. Likewise, the mass transfer of blood-borne constitutents like oxygen or lipoproteins can be affected by the flow patterns in various regions near the artery wall. An imbalance n the mass transfer of these elements can cause either vascular damage or excess accumulation of lipids which can eventually lead to a pathological state in the artery wall.

Proposed Course: (1) Study the flow patterns in these models using the various techniques described above as a function of several flow parameters such as Reynolds number, branch flow ratio, and flow pulse frequency. (2) Correlate these findings with those of our previous experiments on wall shear stress in similar models. (3) Determine the mass transfer coefficients to the arterial wall as a function of various Schmidt numbers under conditions of steady and pulsatile flow. (4) Correlate all hemodynamic evidence with incidence of lesions in experimental animals.

Publications:

Lutz, R.J., Menawat, A., Hsu, L., Zrubek, J.: Fluid Mechanics and Boundary Layer Mass Transport in an Arterial Model During Steady and Pulsatile Flow. In Gross, J. and Tarbell, J. (Chairmen), Biology Rheology and Fluid Mechanics, 74th Annual AIChE Meeting, New Orleans, Louisiana, 1981.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10043-04 BEI

PERIOD COVERED
October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)
Fiber Optic Probes/Oxygen

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI: J.I. Peterson Chemist BEIB, DRS

COOPERATING UNITS (if any)
H-IR-MH

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Chemical Engineering

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
.70	.70	

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES X (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

The development of an implantable fiber-optic PO_2 probe for clinical and physiological measurements has continued through this year. The fiber-optic pH probe we developed earlier i a general model for the current design. The PO_2 probe is an optical device for measuring oxygen tension in the body, based on oxygen's effect of decreasing the fluorescence of certain dyes.

Objectives: Develop an oxygen sensor for physiological implantation to be used in studies of oxygen transport during exercise, and clinical Po_2 measurements.

Methods Employed: A fiber optic measurement of dye-indicator response to oxygen by fluorescence quenching.

Significance: Po_2 measurements are fundamental to understanding and control of oxygen transport in research and clinical investigations. Measurements on withdrawn blood samples lack convenience, reliability, and relevance to many situations of interest. Indirect estimation of Po_2 using spectrophotometric measurements of hemoglobin oxygenation and the concentration-pressure transfer function (blood oxygen saturation curve) is subject to too many uncertain variables. Development of a fiber optic Po_2 probe would represent a significant advance in the ability to directly and continuously measure blood and tissue oxygen. A satisfactory electrode for general use has never been developed, and the fiber optic approach offers some distinct advantages in small size, flexibility, and safety.

Major Findings and Proposed Course: Previous work involved solving the problems of finding a suitable dys, a suitable support for the dye, and an oxygen permeable containment system, along with evaluation of the performance of probe construction methods.

The current year has been partly devoted to development of an associated instrumentation system for the probe, as it became evident that further development and evaluation of the probe depended on this. Following this, the latter part of the year has mainly involved work to improve the probe and test its suitability for use under physiological conditions. This will continue into the next year.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10050-03 BEI

PERIOD COVERED

October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)

Positron Emission Tomography Scanner

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	G. DiChiro	Section Chief	SN NINCDS
OTHER:	R.A. Brooks	Senior Staff Fellow	SN NINCDS
	V.J. Sank	Research Physicist	SN NINCDS
	W.S. Friauf	Electronics Engineer	EEES BEIB DRS
	S.L. Leighton	Mechanical Engineer	MES BEIB DRS
	H.E. Cascio	Electronics Engineer	EEES BEIB DRS
	G.L. Hemphill	Electronics Technician	EEES BEIB DRS

COOPERATING UNITS (if any)

SN NINCDS

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

EEES, MES

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:

CHECK APPROPRIATE BOX(ES)

x (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☒ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

A custom PET scanner is being developed to provide compromises between resolution, sensitivity, count rate capability, and cost that are optimal for human neurological research requirements at NIH.

Objectives: Design and have built a PET scanner with higher resolution than other custom or commercial machines, but without excessive compromise of sensitivity or count rate capability.

Methods Employed: The design will feature a large number of BGO detectors more tightly packed in a smaller ring than other designs, with electronic advances to shorten the coincidence window to a minimum, thus easing the random coincidence problem which is aggravated by a small ring. A novel detector motion has been developed to further improve resolution.

Major Findings: System integration of the major sub-systems has been under way for the past year. These sub-systems include the gantry, ring assembly, electronics, computer, display system, and software. Numerous problems have been encountered and resolved. All indications are that the original performance specifications should be realized.

Significance: PET imaging with a variety of positron emitting tracers allows many metabolic processes to be studied spatially. The new scanner will increase the spatial resolution which currently limits the potential of the approach.

Publications:

Brooks, R.A., Sank, V.J., DiChiro, G., Friauf, W.S., and Leighton, S.B.: "Design of a High Resolution Positron Emission Tomograph: The Neuro-PET. Journal of Computer Assisted Tomography 4(1): 5-13, February, 1980.

Brooks, R.A., Sank, V.J., Friauf, W.S., Leighton, S.B., Cascio, H.E., and DiChiro, G.: Design Considerations for Positron Emission Tomography. IEEE Transactions Biomed. Eng. Vol. BME-28, No. 2, Feb. 1981, pp. 158-177.

Invention Reports: Four have been submitted.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10053-03 BEI

PERIOD COVERED
October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)

Membrane Based Sampling Systems for in In Vivo and In Vitro Kinetic Studies

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	P.M. Bungay	Chemical Engineer	BEIB DRS
OTHER:	J.P. Froehlich	Senior Investigator	GRC NIA
	R.L. Berger	Section Chief	LTD NHLBI
	J. Fenstermacher	Section Chief	LCHPH DCT
	R.L. Dedrick	Section Chief	ChES BEIB DRS

COOPERATING UNITS (if any)

Gerontology Research Center-NIA; Laboratory of Technical Development-NHLBI; Laboratory of Chemical Pharmacology-DCT.

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Chemical Engineering

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
1.5	1.0	

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES X (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Synthetic membranes are being utilized in kinetics studies to provide a means for continuous sampling of the liquid phases from systems in which a dispersed particulate phase is suspended in the liquid phase. In one application sampling equipment is being developed for in vitro study of calcium ion transport and calcium-ATPase activity in suspension of sarcoplasmic reticulum vesicles prepared from homogenates of rabbit muscle. In a second application a study of the mammalian blood-brain-barrier permeability is being aided by the development of an apparatus incorporating a sampler in an arteriovenous ex vivo shunt. In the latter plasmapheresis application pooling the plasma filtrate yields a single sample from which the plasma concentration times time integral can be evaluated for a chemical administered to the animal. Such sampling systems can be useful for the study of the kinetics of other fluid phase systems for which a membrane can be found which is permeable to one chemical of interest but impermeable to another necessary reagent or sink. Thus, other applications might be found in the areas of enzyme kinetics, pharmacokinetics, and the membrane transport of vesicle and cell suspensions.

Objectives: The principal objective is the development of the capability for fluid sampling based upon synthetic membrane technology. In many potential applications sampling by filtration or ultrafiltration may be more appropriate than alternative sampling techniques. Ultrafiltration membranes allow the formation of samples representative of the free concentration of small soluble substances. These membranes will retain within the system under study macromolecules and those substances which are bound to them as well as colloidal or cellular components of the system. Other applications may call for the use of larger pore diameter membranes of, for example, macromolecules are to be sampled as well.

Methods Employed: The sampling system generally consists of three elements: (1) a module or modules containing sampling membranes, (2) sample collection equipment, and (3) a means for controlling the rate of production of sample. The membrane module is designed so that the membrane forms a part of the wall of the channel through which the liquid to be sampled flows. Only a small fraction of the liquid is diverted across the membrane to form the sample. The sample is produced as a consequence of a difference in pressure imposed across the membrane. The rate of production of the sample is regulated either by controlling the transmembrane pressure difference or through use of a sample metering pump.

Significance: Membrane sampling is being applied to studies of the transport of calcium ions across sarcoplasmic reticulum (SR). The transport studies are performed in vitro on a suspension of SR vesicles in buffer; the vesicles being created by homogenizing rabbit muscle. The kinetics of calcium uptake by or efflux from the vesicles can be followed by monitoring the appearance or disappearance of calcium from the suspending medium. Also, changes in levels of ATP and inorganic phosphate can be used to infer the kinetics of the calcium dependent membrane ATPase. The membrane in the sampler retains the vesicles (which are thought to be in the range of 0.1-0.5 m in diameter), so that the sample is representative of the suspending media.

A second application concerns in vivo studies of transport across the blood-brain-barrier. The initial objective is the determination of the barrier permeability to selected marker substances. In these experiments a sampler is connected in line with an extracorporeal arteriovenous shunt. By continuously and steadily drawing off a fraction of the shunt flow through the sampler membrane, one can integrate over time the concentration of the marker substances present in the plasma. The value of the integral, together with a determination of the amount of the substance taken up by the brain over the same time interval, permits a determination of a permeability-area transport coefficient for certain substances, such as potassium ion and x-amino isobutyric acid. A membrane which retains blood cells is of use in studies in which the transport of the substance into blood cells is sufficiently slow that the cells cannot be considered in equilibrium with the plasma. Use of ultrafiltration membranes may permit determination of the free concentration - time integral, rather than the integral for total plasma concentration, in circumstances of significant binding to plasma proteins.

The in vivo sampling technique can be applied to other acute pharmacokinetic studies for which the plasma concentration-time integral can be of use.

Major Findings: A premise underlying the concept of filtration sampling is that the marker substance appears in the filtrate (sample) solely because it is carried convectively across the membrane. However, in kinetic experiments in which the concentration of the marker on the upstream side of the membrane changes sufficiently rapidly with time, appreciable marker concentration gradients can be created across the membrane. Marker diffusion across the membrane can diminish or augment the amount of marker present in the sample. If the filtrate flow rate is sufficiently high or the diffusivity of the marker is small the diffusional contribution should be negligble compared to that from convection. We have been simulating the in vivo animal pharmacokinetic experiments using radiolabeled markers and a sheet membrane module in an in vitro set-up. Under the range of conditions investigated the sample has been representative of the rententate for nonbinding markers which suggests that diffusional artifacts should be negligible. We have begun the in vivo experiments using rabbits. The first substance being investigated is sucrose - a neutra nonbinding extracellular marker.

Other Activitites: Sponsored sessions on Synthetic Membrane Technology, national Institutes of Health Instrumentation Symposium, December 10-12, 1980; presented review "Current Applications in Biomedical Research".

Publications:

Dedrick, R.L. and Bungay, P.M. Meeting Report on the Synthetic Membrane Technology Sessions, 1980 National Institutes of Health Instrumentation Symposium

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10055-03 BEI

PERIOD COVERED
October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)

Breath by Breath Analysis of Computer Controlled Exercise Stress Testing

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	L. Thibault	Mechanical Engineer	ACES BEIB DRS
OTHER:	W. Schuette	Chief	ACES BEIB DRS
	T. Talbot	Mechanical Engineer	ACES BEIB DRS
	H. Tipton	Mechanical Engineer (Tech.)	ACES BEIB DRS
	R. Winslow	Sr. Scientist	IR-CL-NHLBI

COOPERATING UNITS (if any)
IR-CL-NHLBI

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Applied Clinical Engineering

INSTITUTE AND LOCATION
DRS, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
0.5	0.4	0.1

CHECK APPROPRIATE BOX(ES)

X (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

In recent years exercise stress testing has become an important diagnostic tool. Most testing of this type is confined to cardiac studies. This system has been developed in order to assess the ability of the subject to transport and exchange oxygen and carbon dioxide between the atmosphere and the cells of the body. A large number of pathophysiologic states limit one's ability to perform these functions efficiently. With this system the anaerobic threshold of the subject during exercise can be detected non-invasively by breath-by-breath respiratory analysis. Oxygen Uptake, Carbon Dioxide Production, Respiratory Minute Volume, Respiration Rate, Heart Rate, and Respiratory Quotion are displayed as a function of Work Rate.

Z01 RS 10055-03 BEI

Objectives: To develop a system to analyze the respiratory quotient vs. work rate curve during exercise stress testing in order to determine the anaerobic threshold.

Methods Employed: A Tektronix 4051 programmable calculator and custom designed synchronous integrators and multiplexor has been used to produce breath-by-breath analysis of respiratory quotient as a function of work rate.

Significance: Correlation of the onset of anaerobic metabolism with work level provides a useful clinical measure of the general condition of the hematology patients under study. This method provides a better means of evaluating the efficacy of therapeutic measures.

Proposed Course: To add a pressure transducer to the mouthpiece in order to obtain respiratory power and work.

Publications:

Talbot, T.L., Thibault, L.E., Schuette, W.H., Winslow, R.M., and Tipton, H.W.: Breath-by-breath gas analysis during exercise stress testing. Advances in Bioengineering, 1979.

Schuette, W., Thibault, L., Talbot, T., and Tipton, H.: Synchronous integration - a method for the rapid determination of the mean value of pulsatile physiological signals. Proc. AAMI 15th Annual Meeting, San Francisco, April 13-17, 1980, p. 184.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10060-02 BEI

PERIOD COVERED
October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)

Analytical High Voltage Electron Microscopy and Image Analysis

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	R.D. Leapman	Physicist	BEIB DRS
OTHER:	C.E. Fiori	Physical Scientist	BEIB DRS
	A.F. LeRoy	Chief, Micro. Group	BEIB DRS
	E. Silbergeld	Neurotoxicologist	ETB IRP NINCDS
	J.L. Costa	Staff Physician	CNB NIMH
	K.E. Gorlen	Electronics Engineer	CSL DCRT
	E. Pottala	Electronics Engineer	LAS DCRT
	C.R. Swyt	Physicist	BEIB DRS
	L.K. Barden		CSL DCRT
	J.S. DelPriore		CSL DCRT
	P.S. PLexico		CSL DCRT
	M.A. Douglas		LAS DCRT
	C.C. Gibson	Electronics Engineer	BEIB DRS
	R.L. Ornberg		
	T. Reese		

COOPERATING UNITS (if any)

Computer Systems Laboratory, DCRT, NIMH, NINCDS; NINCD

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Microanalysis Group

INSTITUTE AND LOCATION
DRS, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
3.0	2.5	

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

A number of features have been added to the Hitachi H700H TEM-STEM electron microscope and to the Electron Energy Loss Spectrometer (EELS). New alignment controls have improved the signal and energy resolution of the EELS making possible the study of some biological samples. These include dense bodies contained in blood platelets and inclusions in bacteria, where the light elements N and O as well as P and Ca have been detected. The addition of a liquid nitrogen cold stage has enabled 30nm diameter areas to be proved without contamination build-up, which had previously been a serious problem.

An annular detector has been installed for dark-field STEM imaging and it is planned to use this for contrast enhancement in unstained samples. Descanning of the EELS spectrometer has almost been completed and this will allow elemental mapping. Images will be digitized, stored on disk and displayed on a DeAnza graphics system linked to the PDP 11/60 computer. Considerable software has already been developed to process EELS and EDX spectra, which can now be loaded automatically into the main computer from the Kevex 7000. Other interfacing to the H7000H microscope should soon permit direct computer control of the EELS spectrometer as well as various new imaging modes to be implemented.

Objectives: To investigate how Electron Energy Loss Spectroscopy and Energy Dispersive X-ray spectroscopy can be exploited to carry out elemental microanalysis, and to establish how these methods can be combined with new imaging techniques.

Experimental Techniques: A 200 keV electron microscope is utilized to probe microvolume of thin biological samples. Elements are detected by recording their characteristic ionizations either using EDX where the de-excitation of the ionized atom causes x-ray emission, or using EELS where the ionization events are observed in the energy losses of the incident electrons.

Significance: EEELS permits the microanalysis of the light elements which are difficult to detect by any other means. EDX spectroscopy is complementary to EELS and together the techniques allow the investigation of a wide range of biological problems.

Proposed Course: To study in detail the application of Analytical Electron Microscopy in biology.

Publications:

Leapman, R.D. and Swyt, C.R.: Microanalysis of Ca and P biology using EELS. Proc. 39th EMSA Meeting, Atlanta (1981) Baton Rouge, G.W. Bailey, (Ed.), p.636.

Leapman, R.D. and Swyt, C.R.: A practical method for removing plural scattering from core edges. Proc. 39th Annual EMSA Meeting, Atlanta (1981) Baton Rouge, G.W. Bailey, (Ed.), p. 196.

Grunes, L.A., Leapman, R.D., Ray, A.B. and Silcox, J.: Some Observations on Core Edge Fine Structure and Orientation Dependent Effects in Inelastic Electron Scattering. Proc 39th Annual EMSA Meeting, Atlanta (1981), Baton Rouge, G.W. Bailey (Ed.), p. 178.

Leapman, R.D., Grunes, L.A., Fejes, P.L. and Silcox, J.: Extended Core Edge Fine Structure in Electron Energy Loss Spectra. In "EXAFS spectroscopy: Applications and Techniques", B.K. Teo and D.C. Joy (Eds.), Plenum Press, New York (1981), pp. 217-240.

Leapman, R.D. and Grunes, L.A.: Anamolous L_3/L_2 White-Line Ratios in the 3d Transition Metals. Physical Review Letters 45:397 (1980).

Leapman, R.D. and Grunes, L.A.: Microcharacterization of some Metals and their oxides using EELS Fine Structure. Proc. 7th European Congress on Electron Microscopy 3:70, The Hague (1980).

Grunes, L.A. and Leapman, R.D.: Optically Forbidden Excitation of the 3s subshell in the 3d transition elements. Phys. Rev. B22:3778 (1980).

Leapman, R.D. and Swyt, C.R.: EELS under conditions of plural scattering. Analytical Electron Microscopy - Proceedings of AEM Workshop, Vail, R.M.Geiss (Ed.)

Rez, P and Leapman, R.D.: Core loss shape and cross section calculation. Analytical Electron Microscopy - Proceedings of AEM Workshop, Vail, R.H. Geiss (Ed.)

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10061-02 BEI

PERIOD COVERED
October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)
Automated Scanning Electron Beam X-ray Microanalysis

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	C.E. Fiori	Physical Scientist	BEIB DRS
OTHER:	A. LeRoy	Chief, Micro. Group	BEIB DRS
	C.R. Swyt	Physicist	BEIB DRS
	K.E. Gorlen	Electronics Engineer	DCRT
	C. Merril	Biochemist	L GCB NIMH

COOPERATING UNITS (if any)
CSL, LAS, DCRT

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Microanalysis Group

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
2.0	1.5	

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Due to budgetary constraints imposed during this reporting period it has not been possible to acquire the necessary hardware to interface the microprobe to out PDP 11-60 computer as projected in the last report. Consequently the emphasis of our work shifted to casting into computer programs those algorithms required to convert raw x-ray intensity data into chemical concentrations. These programs include a procedure to unravel spectral overlap, a Monte Carlo procedure to examine the production of x-rays from irregular specimens such as liquid micro-droplets and a procedure to perform matrix corrections with a strong emphasis on biological applications. The programs are required to obtain quantitative chemical information from biological samples and are not generally available. The program to correct for the effects of spectral overlap has been completed and reported on. The other two programs are in advanced stage.

Work has been done on developing a new class of standard reference material for biological microanalysis. The material is comprised of Lithium borate glass doped with biologically relevant elements such as Mg, Al, Si, P, S, Cl, K, Ca . . . The glass has the interesting property of having a nearly identical matrix as biological material in terms of the electron and x-ray physics. Consequently, more accurate analysis is possible. A paper has been written on this work and has been accepted by the Journal of Microscopy.

Preliminary collaborative work has been don with Dr. Carl Merril of the Laboratory of General and Comparative Biochemistry, Institute of Mental Health. This work involves the determination of trace metals in the protein spots isolated by two dimensional gell electrophoresis. This work will continue.

Objectives: To provide a capability of performing elemental microanalysis on both bulk and thin biological specimens utilizing focussed electron beam induced X-ray spectroscopy.

Methods Employed: A focussed 2-50 keV electron beam is utilized to photoionize microvolumes (containing as small as 10^{-18} grams of matter) of biological specimens. By performing X-ray spectroscopy utilizing Bragg angle X-ray spectrometers, on the X-rays leaving the photoionized volume of the specimen it is possible to perform elemental microanalysis.

Significance: Electron beam microanalysis permits the solution of certain biological problems which would be difficult, or impossible, by other means.

Proposed Course: To apply the technique to biological research and to study in detail the problems involved in this application.

Publications:

Fiori, C.E., Swyt, C.R. and Gorlen K.E.: Application of the Top-Hat Digital Filter To A Nonlinear Spectral Unraveling Procedure in Energy Dispersive X-ray Microanalysis. Proc. of Microbeam Analysis Society. 1981, pp. 320-324.

Fiori, C.E. and Newbury, D.E.: The Operation of Energy Dispersive Detectors in the Analytical Electron Microscope. Analytical Electron Microscopy. R. Geiss (Ed.), San Francisco Press, In press.

Fiori, C.E., Gorlen, K.E. and Gibson, C.G.: Comments on the Computerization of an Analytical Electron Microscope. Proc. 39th Annual Meeting of EMSA, 1981, pp. 246-249.

Fiori, C.E.: Electron Beam Microanalysis: Several Instrumental Developments Germane to Biology. Journal of Histo-Cyto Chemistry, 29, pp. 1029-31, 1981.

Fiori, C.E. and Blackburn, D.B.: Low Z Glass Standards for Biological X-ray Microanalysis. Accepted by Journal of Microscopy.

Heinrich, K.F.J., Newbury, D.E., Myklebust, R.L. and Fiori, C.E. (Eds.), Energy Dispersive X-ray Spectrometry. National Bureau of Standards, Special Publication 604 U.S. Goverment Printing Office, pp. 1-443.

The following four papers in the preceding book:

Fiori, C.E., Myklebust, R.L. and Gorlen, K.: "Sequential Simplex: A Procedure for Resolving Spectral Interference in Energy Dispersive X-ray Spectrometry", p. 233.

Fiori, C.E., Newbury, D.E. and Myklebust, R.L.: "Artifacts Observed in Energy Dispersive X-ray Spectrometry in Electron Beam Instruments - A Cautionary Guide", p. 315.

Myklebust, R.L., Fiori, C.E. and Heinrich, K.F.J.: "Spectral Processing Techniques in a Quantitative Energy Dispersive X-ray Microanalysis Procedure (FRAME C), p. 365.

Fiori, C.E. and Swyt, C.R.: "Energy Dispersive Detectors - A Bibliography (1981)", p. 417.

Mannis, M.J., Fiori, C.E., Krachmer, J.H., Rodriquez, M.M. and Pardos, G.: Keratopathy Associated with Intra-Corneal Glass", Archives of Opthalmology, Vol. 99, May 1981, pp. 850-852.

Goldstein, J.I., Newbury, D.E., Joy, D.C., Fiori, C.E., Echlin, P. and Lifshin, E.: Scanning Electron Microscopy and X-ray Microanalysis: A Text for Biological, Geological and Materials Scientists. Plenum Press, (In Press).

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10062-02 BEI

PERIOD COVERED

October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)

IEEE-488 General Purpose Interface Bus Program Development

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI: T.R. Clem Electronic Engineer EEES BEIB DRS

COOPERATING UNITS (if any)

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Electrical and Electronic Engineering

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
0.3	0.2	0.1

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES x (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

The ability to produce instrumentation systems using several individual instruments interconnected via the IEEE-488 General Purpose Interface Bus (GPIB) is being developed. With the cooperation of the BEIB-SERP a variety of bus-compatible instruments is being acquired to complement this ability.

Z01 RS 10062-02 BEI

Objectives: Develop expertise in the Branch in the use of IEEE-488 GPIB-compatible instruments and controllers. Recommend types of bus-compatible instruments for acquisition by the BEIB-SERP.

Methods Employed: Prototype or temporary systems are assembled from equipment available in the rental program. Prototype systems are assembled to prove feasibility of techniques prior to the design of dedicated systems. Temporary systems are used either to satisfy short-term instrumentation needs or to solve problems which require a quick response. A system was configured in the laboratory of Dr. Phil Ross, LMB, NIADDK, to temporarily replace a piece of equipment that has failed and needed repairing. By being able to set-up a bus-oriented system in less than two days as a substitute, there was virtually no disruption to the experiments in progress while the primary equipment was being repaired.

Significance: The capability of assembling an instrumentation system with a controller and GPIB-controlled instruments allows the EEES to provide a rapid response to an investigators call for instrumentation. By assembling a system with "off-the-shelf" instruments from the SERP, the cost of a special-purpose measurement or control system can be kept quite low. If the experiment is a short-term project the instruments can be returned to the SERP with virtually no expenditures, by the investigator, for equipment.

Proposed Course: Maintain state-of-the-art capability in the field of bus-compatible instruments and controllers. Seek to make this capability better known and understood around NIH.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10063-02 BEI

PERIOD COVERED
October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)
Digital Thermistor Thermometer

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	T.R. Clem	Electronics Engineer	EEES BEIB DRS
OTHER:	R. Berger	Section Chief	LTD NHLBI

COOPERATING UNITS (if any)
LTD, NHLBI

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Electrical and Electronic Engineering

INSTITUTE AND LOCATION
DRS, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
0.2	0.1	0.1

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

High resolution and high accuracy thermistor thermometers, using microprocessors as control components, are being developed. These units are suitable for process control and data logging uses in the laboratory.

PHS-6040
(Rev. 2-81)

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10064-02 BEI

PERIOD COVERED

October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)

Indirect Blood Pressure Measurements in Laboratory Animals Using Oscillometry

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	E.C. Walker	Mechanical Engineer	BEIB DRS
	J.E. Pierce	Chief, LAMSS, OD	NHLBI

COOPERATING UNITS (if any)

NHLBI

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Applied Clinical Engineering

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
1.5	1.0	0.5

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Currently there are no reliable indirect methods of measuring blood pressure in dogs. Traditional techniques, used in humans, are unsatisfactory primarily because they require the placement of a transducer over the artery being monitored.

Because of the unreliability of traditional techniques we have been investigating a technique called oscillometry. Oscillometry is a method of measuring blood pressure by analyzing the pulse pattern of the cuff pressure oscillations.

In practice, a cuff is placed around a limb and inflated to a pressure above systolic and then slowly deflated. While the cuff is being deflated the amplitude of oscillation in cuff pressure, produced by the arterial pulse beneath the cuff, is monitored. Systolic pressure is indicated by the first significant increase in oscillation amplitude. Diastolic pressure is indicated as the lowest cuff pressure at the point of maximum oscillation in cuff pressure. Currently most investigators using this technique take the point of maximum oscillation to indicate mean arterial pressure.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10065-01 BEI

PERIOD COVERED

October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)

Transient Response of Micro-Calorimeters Using R-C Analysis

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	C. P. Mudd	Biomedical Engineer	BEIB, DRS
OTHER:	R. L. Berger	Section Chief	LTD, NHLBI

COOPERATING UNITS (if any)

LTD, NHLBI

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Mechanical Engineering

INSTITUTE AND LOCATION

National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES x (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

The behavior of microcalorimeters lies between that of true adiabatic or bomb calorimeters and isothermal calorimeters. The location between these extremes depends upon a compromise involving many criteria but most importantly, time constant and sensitivity. The use of an R-C model of the system and Laplace transform techniques will allow us to study the transient behavior of the system to a variety of inputs, and to achieve optimized performance for specific applications of the calorimeter.

Objective: The objective of the analysis is to develop a model which can be used to predict the calorimeter's performance. If the model predicts the calorimeter's response to pulse and step inputs, it can be used as a design aid in subsequent redesigns and optimizations for specific applications.

Significance: To date, the model agreement with experimental data for pulse and step inputs is very good. In addition, the model has shown that the air gap between the cell and cell holder is the largest source of uncertainty in the instrument. Thus, the model has identified a key parameter as the major source of error in the calorimeter.

Proposed Course: By using the model, we have designed a new configuration for the sensor which eliminates the air gap by utilizing one thermopile instead of two. The new design should have greater sensitivity than the two thermopile configuration with no increase in rise-time.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10066-02 BEI

PERIOD COVERED

October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)

Egyptian Training Project

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	C. P. Mudd	Biomedical Engineer	BEIB, DRS
OTHER:	H. W. Metz	Assistant Branch Chief	SES BEIB DRS

COOPERATING UNITS (if any)

RIS, BEIB, DRS

LAB/BRANCH

SECTION

Mechanical Engineering

INSTITUTE AND LOCATION

National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

The development of a system for transferring the training of Egyptian engineers in equipment repair from NIH to Egypt. The goal is a completely self-sufficient training center in Egypt for recruitment and training of scientific equipment repair personnel. This project is specifically concerned with the development of a 12 week course in basic instrumentation and electronics for scientific equipment.

Z01RS10066-01BEI

Objective: During Phase I of this project, several repair centers were organized and set up in Egypt. The personnel were brought to NIH for training and then sent to the centers. In Phase II, the emphasis will be on developing a facility in Egypt which assumes the training role. At the end of Phase II, the facility should be completely self-sufficient and staffed with Egyptian training personnel.

Significance: At the conclusion of Phase II, the role of NIH in the training process will end and the Egyptian facility must be capable of operating independently.

Proposed Course: A condensed, preliminary version of the training course will be presented in Egypt in October-November of 1981. The purpose is the selection of engineers to return to NIH to be trained in presenting the complete course in Egypt.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10069-02 BEI

PERIOD COVERED
October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)

Automated Test Apparatus and Data Handling System for Patient Electrical Safety Program

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	C. Wooten	Electronics Engineer	EEES BEIB DRS
OTHER:	H. Cascio	Electronics Engineer	EEES BEIB DRS
	W. Friauf	Section Chief	EEES BEIB DRS
	H. W. Metz	Chief	RIS BEIB DRS
	W. Connoley	Supervisor	RIS BEIB DRS
	R. Corsey	Electronics Engineer	ACES BEIB DRS
	L. Martin	Programmer	DMB CR
	S. Soroka	Programmer	DMB CR

COOPERATING UNITS (if any)
RIS, DCRT

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Electrical and Electronics Engineering

INSTITUTE AND LOCATION
DRS, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
2	1	1

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

A microprocessor based automatic test set for checking the safety of electrically operated patient care equipment has been designed and built. Test results are stored on cassette tapes which are compatible with the IBM/370 computer. Through discussions with DCRT, a program has been written to input the data from the tapes and file it and manipulate it to provide better documentation and analysis for the safety program.

Z01 RS 10069-02 BEI

Objectives: The objective is to provide an automated test set which can safely and accurately measure the parameters of devices in their operating environment. Also, the objective is to facilitate the handling, storage, and presentation of this data so that the safety of the equipment being tested can be better evaluated and statistical and trend analysis of past and present data can be done.

Methods Employed: Using microprocessor technology, manual input and bar code scanner input can be interfaced to the test set to provide identification of the equipment and annotations on the test itself. A tape transport stores all this data on cassettes.

Significance: By monitoring the results from the safety test data, problems in the safety and everyday operation of the equipment can be detected or even predicted to prevent hazards to the patients.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10071-01 BEI

PERIOD COVERED
October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)
Fiber Optic Probes for Cardiac Instrumentation

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	S.R. Goldstein	Chief	MES BEIB DRS
OTHER:	R. Levin	Biomedical Engineer	MES BEIB DRS
	D. Markle	Biomedical Engineer	MES BEIB DRS
	R. Patterson	Senior Investigator	NHLBI

COOPERATING UNITS (if any)
Cardiology Branch, NHLBI

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Mechanical Engineering

INSTITUTE AND LOCATION
DRS, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
.2	.2	

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

The use of miniature fiber optic probes for acute insertion into canine myocardium is being investigated. Measurements of local blood flow and local capillary permeability in the presence of various interventions are contemplated. Practical problems dealing with insertion into tissue, validation of readings, elimination of motion artefacts, and overall characterization of in-vivo performance are of major interest.

Objectives: Perfect and enhance techniques developed for the pH probe (described elsewhere in this years report) utilizing miniature fiber optic probes to measure tissue perfusion and capillary permeability in canine hearts in vivo.

Methods Employed: Utilize miniature fiber optic probes to perform measurements in acute dog experiments. Perform tests to determine practical problems, e.g., breakage, tissue insertion, artefacts, calibration difficulties, elimination of motion artefacts, zero shifts, hysteresis, etc. Develop solutions to above problems using improved probes and signal processing instrumentation.

Significance: At present there are no completely satisfactory techniques for measuring local perfusion, and capillary permeability in-vivo in an "on-line" manner. Perfection of these measurements would represent a great advance in the techniques presently available to experimental cardiologists and other biomedical researchers not only in terms of convenience, but also in terms of opening up many new areas of investigation.

Major Findings and Proposed Course:

(a) Perfusion measurements are feasible, i.e., there is acceptable signal-to-noise ratio. Motion artefacts must be eliminated and an approach is being investigated. Validation using microspheres will be performed once an automatic gain ranging system is implemented so that traces can be reliably obtained. Various flow limited fluorescent markers in addition to fluorescein will be sought. A data acquisition system using a Tektronix 4052 terminal is being developed.

(b) Capillary permeability studies will be investigated after the perfusion techniques has been perfected. Fluorescent labeled compounds of appropriate molecular weight (possibly fluorescein labeled albumin) will be sought and used.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10072-02 BEI

PERIOD COVERED
October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)

Clinical Evaluation of Membrane Oxygen Dissociation Curve Analyser

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	W.H. Schuette	Chief	ACES BEIB DRS
OTHER:	L. Thibault	Mechanical Engineer	ACES BEIB DRS
	H. Tipton	Mechanical Engineer	ACES BEIB DRS
	D. Lees	Staff Anesthesia	CC NIH

COOPERATING UNITS (if any)
CC - NIH

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Applied Clinical Engineering

INSTITUTE AND LOCATION
DRS, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
2	1.5	.5

CHECK APPROPRIATE BOX(ES)

☒ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

A fully automated, computer controlled method for determining and plotting the entire hemoglobin-oxygen dissociation curve on less than .5 cc of blood has been developed and is being introduced to clinical practice. A micro-computer controls the calibration of the system as well as the initial desaturation and subsequent saturation of the blood specimen.

Methods Employed: Initially the specimen is desaturated by exposure to a CO_2/N_2 mixture. Once the pO_2 falls below 0.5 torr, the computer automatically starts the saturation with a mixture of oxygen and CO_2. Gas is exchanged with the sample in a reaction cell across a silicone rubber membrane which mechanically separates the two phases. The sample solution is contained within an annular region formed by the cylindrical membrane and the sample cavity walls where it is stirred by a thin-walled cupshaped stirrer, magnetically coupled to an outside motor-driven rotor. A conventional polarographic oxygen electrode continuously monitors the partial pressure of oxygen in the sample. The amount of oxygen delivered to the sample is calculated by integrating the diffusion equation and the measured pO_2 gradient across the thin silicone membrane.

Major Findings: The described system appears to be a simple and reliable way of obtaining the hemoglobin-oxygen dissociation curve for clinical applications.

Publications:

Lees, D.E., Schuette, W.H., Thibault, L.E., Kim, Y.D., Tipton, H.E. and MacNamara, M.B.: Computerized Determination of Oxygen Dissociation Curve. Anesthesiology, Vol. 53, No. 3, September 1980.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10073-02 BEI

PERIOD COVERED
October 1, 1980 to September 30, 1981.

TITLE OF PROJECT (80 characters or less)

Secondary Emission Experimental Mass Spectrometer

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	L. Kelner	Visiting Associate	BEIB DRS

COOPERATING UNITS (if any)

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Microanalysis Group

INSTITUTE AND LOCATION
DRS, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
0.3	0.3	

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Secondary Emission Mass Spectrometer (SEMS) will be build by Gatan, Inc. and Extranuclear Labs and owned by BEIB Rental Program. It is anticipated that this facility will contribute to research programs in a number of Institutes, specifically NIMH (S. Markey) and NHLBI (H. Fales). The SEMS will have the following features:

(1) Ultra-high Vacuum System - up to 10^{-9} Torr.

(2) Rapid linear motion multi-specimen holder permitting normal and transmission SIMS modes of operation.

(3) Energy analyzed ion gun (.05 - 10 kV) with deflector, pulser, and rastering. The ion gun will allow us to bombard the specimen with ions free of neutrals or by energetic neutrals only.

(4) Quadrupole Ion Storage Device (QUISTOR) and electronics.

(5) Simultaneous CI/EI Ionizer to allow simultaneous spectra in both CI and EI modes of operation.

(6) Secondary Ion Mass Spectrometer in both Reflected (SIMS) and transmission (TSIMS) modes.

(7) Three dimensional mass spectrometry (MS/MS/collision cell double quadrupole system).

(8) Secondary Electron Emission Cell for negative ions studies.

(9) This System will permit us to add later a Sputter Induced Photon Spectrometer to detect the light emitted by sputtering particles. Simultaneous SIPS and SIMS analysis and direct viewing by optical microscope of the target will be available.

The system will feature an MS/MS double quadrupole system. In the last year, the MS/MS technique has been proven to be effective in analyzing mixtures of organic compounds and on many occasions may supplement a GC/MS technique, which is hardly applicable in SIMS. This is a very important feature of the system making it a unique and important for biological applications.

The SEMS will permit us to study secondary emission processes on surfaces under bombardment by electrons, ions, and neutral particles in connection with ionization of organics (compounds of biological interest), to detect sputtered secondary ions and transmitted ions (positive and negative), to detect optical emission of sputtered particles, and to store ions in order to obtain higher sensitivity and selectivity of the mass spectrometric analysis.

The system will be based on Gatan's model 591 SIPS-SIMS Scanning Ion Microbe; various components of the instrument will be modified, adapted and designed to match to one another.

Several components of the system have been already purchased. This includes Extranuclear's plus-SIMS quadrupole mass spectrometer, multi-flange ionization chamber and electron-gun power supply. The ionization chamber was designed this year in cooperation with MDC Manufacturing Co. It is expceted that the instrument will be assembled and tested at Gatan's facility in Pittsburgh and then delivered to NIH sometime this next spring (April-May, 1982).

Thermal Stability in the Ion Source

Other activities under project involved the study of the thermal stability of various organic compounds, including cholesterol, cholestane, cortisole, cortisone, and several epoxides. Styrene Oxide (C_8H_8O) and N-(2,3-Epoxypropyl) phthalamide ($C_{11}H_9NO_3$) were chosen for further investigation as references to determine thermal decomposition in ion sources. Preliminary results suggested that N-(2,3-Epoxypropyl) phthalamide may be used for this purpose in the temperature range 100-300°C in the ion source, by detecting the ratio of the fragment $(M-43)^+$ and M^+(molecular peak). Styrene Oxide may be useful to detect metal chorides formed in the interface between GC and MS.

La B_6 Cathodes Development

The other development is in the field of cold emitters and designing more effective emitters or cathodes for MS ion sources. LaB_6 polycrystalline and single crystal cathodes are developed in cooperation with Kimball Physics for LKB-9000, LKB-2091, MS-9 and Finnigan 4000 instruments. Experimental work is in progress to determine the efficiency and feasibility of applications of these cathodes in mass spectrometry.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS I0074-02 BEI

PERIOD COVERED
October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)
Study of analytical applications of QUISTOR

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	L. Kelner	Visiting Scientist	BEIB DRS
OTHER:	S. Markey	Chemist	LCS NIMH

COOPERATING UNITS (if any)
LCS NIMH

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Microanalysis Group

INSTITUTE AND LOCATION
DRS, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
1.0	1.0	

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

The quadrupole ion store (QUISTOR) or three dimensional ion trap has received little attention among analytical chemists compared to the quadrupole mass filter or two dimensional quadrupole. This is in part due to the fact that QUISTOR primarily has been developed, studied, and used by physicists as partial and total pressure analysers and residual gas analysers and most recently as electronically controlled ion-molecule reaction chambers. Recent works by G. Lawson, R.F. Bonner and R. March employing a three dimensional quadrupole ion trap as an ion source for a mass spectrometer has opened new avenues for the QUISTOR as an analytical tool. The QUISTOR is expected to be more compact, the resolution of the instrument would not be mass dependent as for quadrupoles, and the sensitivity of the device, specifically when detecting single ions, may be improved compared to a quadrupole mass spectrometer combined with a conventional ion source.

The Quadrupole Ion Store was constructed and machined from stainless steel, specifications for the driving electronics have been established, RF-generator modified by Exranuclear Labs. will be used to power the QUISTOR, pulse electronics will consist of a Boxcar Averager and Gated Integrater by EG&G, two pulse generators by HP, X-Y Recorder and Tektronix Oscilloscope.

The budget and financing for QUISTOR electronics have been approved. Gatan, Inc. will incorporate the QUISTOR feature in the SEMS instrument.

Objectives: To develop a QUISTOR-mass spectrometer combination and to study the possible applications in analytical mass spectrometry.

Methods Employed: A three dimensional quadrupole electric field will be used to store ions of interest. This field will be formed by three electrodes of a hyperbolic geometry made of stainless steel, which will consist of two "endcaps" and one central ring. The electron gun will be used to ionize molecules of compounds to be studied. The RF-electric field will be applied to a ring electrode and creation and ejection pulses to the end-caps.

Significance: Development of a three-dimensional ion store and its application in mass spectrometry may result in improvements of detection capabilities of existent instruments and may increase limits of detection of compounds of biological interest.

Proposed Course: Construct the driving electronics and detection system for the QUISTOR. Test the device and study its storage capabilities. Interface the quadrupole ion trap with the gas inlet sysem and the gas chromatograph. Employ different types of electron emitters: hot filaments, field emitters, cold cathodes and find the most suitable emitter for the proposed device. Study the applicability of the QUISTOR to mass spectrometric analysis of drugs and other compounds of biological interest.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10075-02 BEI

PERIOD COVERED
October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)

Development of a new method for resolving power measurement

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	L. Kelner	Visiting Scientist	BEIB DRS

COOPERATING UNITS (if any)

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Microanalysis Group

INSTITUTE AND LOCATION
DRS, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
1.0	1.0	

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Decachlorobiphenyl and decabromobiphenyl have been analyzed under positive and negative ion chemical ionization and positive ion electron impact conditions for the purpose of using these compounds as references to evaluate the resolving power of mass spectrometers in a wide mass range (M/Z 100-1000). Molecular clusters and some fragments have been detected with different types of mass spectrometers: magnetic sector as well as quadrupoles, including A.E.I. MS-9, LKB-9000, LKB-2091, Finnigan 3200 and Finnigan 4000. The criteria to determine the resolving power have been found based on the measurement of the minima of two adjacent peaks of the molecular cluster of DCB or DBB. Molecular clusters for DCB and DBB were determined theoretically by plotting the individual ions which constitute each profile at the desired resolution using a standard Gaussian distribution of intensities, and then summing the individual ions with the weighting factors derived from the theoretical statistical isotope distribution ratios of carbon, chlorine, and bromine. By comparing the theoretical values of minima vs. resolution with the experimentally found values of minima between the same two adjacent peaks, the resolving power of a given mass spectrometer can be determined. The method

developed here and the reference compounds DCB and DBB will be recommended to manufacturers and users of mass spectrometers as an easy and accurate way to estimate the resolving power of their instruments both for instrument acceptance and as a routine check-out.

Experimental data for the measurement of the resolving power of different types of mass spectrometers have been analyzed. The inlet system to introduce DCB & DBB into the ion source region has been designed in cooperation with Vacuumetrics, Inc. The availability of financing ($52,000) will determine the continuation of this project.

Objectives: To develop a method to measure the resolving power of various types of low resolution mass spectrometers which will be easier, faster and require less effort than the conventional methods.

Methods Employed: Theoretical values of ion abundances for molecular clusters of decachlorobiphenyl and decabromobiphenyl will be used to determine the resolving power of mass spectrometers by comparing them with the experimental values of minima between two adjacent peaks in the molecular cluster.

Major Findings: The calibration curves MIN=f(R) have been found for molecular clusters of DCB(M/Z 498) and DBB(M/Z 944). The comparison between the theoretically derived MIN values and the experimental data show good agreement between observed and calculated values in the resolution range of 150-500 for DCB and 300-900 for DBB. Thus the two compounds cover the useful range of a low resolution mass spectrometer, i.e., 150-900. It also has been found that DBB may be used as a sensitivity test reference for quadrupole mass spectrometers in a high mass range (600-1000). It can be done by comparing intensities of the peaks centered at M/Z 944 and M/Z 784. Their ratio should be about 0.5.

Significance: A simple method to determine the resolving power of mass spectrometers has been developed. The method can be used in all types of mass spectrometers and with different ionization techniques (electron impact, chemical ionization, positive or negative ions, etc.). The method will be beneficialy to all mass spectrometry users and may improve the specifications of the instruments at their acceptance.

Proposed Course: The inlet system for DCB and DBB will be manufactured by Vacuumetrics and evaluated for applications in organic mass spectrometry by NIH.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10078-01

PERIOD COVERED

October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)

Picosecond Spectroscopy

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	P. Smith	Visiting Scientist	BEIB DRS
OTHER:	G. Liesegang	Senior Staff Fellow	LTD NHLBI
	R. Berger	Chief, Sect. of Biophys. Inst	LTD NIHBI
	H. Cascio	Electronics Engineer	BEIB-DRS

COOPERATING UNITS (if any)

LTD NHLBI

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Electrical and Electronic Engineering

INSTITUTE AND LOCATION

National Institutes of Health, Bethesda, Md. 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
3.0	2.5	0.5

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

A picosecond spectrometer has been developed. Single pulses 6 ps in duration are obtained from a neodymium laser at wavelengths of 530 nm and 1.06 u. Simultaneous generation of a white light continuum provides a synchronous monitor source. A vidicon detector has been fully characterized in the pulsed mode of illumination and a technique developed to significantly improve the linearity of response available from a vidicon.

Objectives: To establish a picosecond spectrometer at NIH for the study of the rapid transients occurring in biological molecules. The understanding of these transients is a prime import in elucidating the mode of action of these molecules.

Major Findings: The major emphasis of the picosecond laser spectroscopy project has been directed toward obtaining a complete understanding of the vidicon detector output. The emphasis on this aspect of the project cannot be overstated when it is considered that results obtained otherwise would not stand scrutiny and be qualitative at best. As is outlined below, a significant contribution has been made to the vidicon detector field in this regard.

A Princeton Applied Research Model 1254B SIT Vidicon and 1216 Vidicon controller have been interfaced to a DECLAB-11/MNC computer system. Testing of the OMA revealed a non-linear vidicon output response to the incident pulsed illumination level. It was determined that the factor affecting this non-linear response was the variable recharging rate of the vidicon surface at medium to low light levels. It was also observed that all vidicon scanning parameters alter this response and a careful calibration of the vidicon must be carried out for a particular set of scan parameters, if the OMA is to be used in pulsed spectroscopic applications.

Careful calibration of the vidicon is highly impractical; a prepare-expose-read cathode voltage switching technique has been devised which substantially improves the output linearity of a SIT vidicon in the pulsed illumination mode of operation. This technique now allows quantitative usage of the vidicon in pulsed spectroscopy. This technique is being incorporated into PAR OMA systems as well as numerous spectroscopic systems.

The picosecond laser system is now fully operational. Overlap of the time-dispersed continuum from the echelle and the 530 nm photolysis beam has been established using a carbon disulphide cell and the zero time segment identified. These segments are well resolved on the vidicon. The response of the spectrometer is currently being investigated by studying the known relaxation of the dye azulene; the characteristics of other dyes, not previously studied are being investigated. Electronic synchronization of the firing of laser system at the end of the last prep frame of the vidicon was achieved using an electronic circuit which features opto-isolators. These protect the vidicon controller and data acquisition system from the rapid transients associated with the laser firing and pulse selection. The cyrogenic system has been received and a sample holder has been manufactured for this unit.

Proposed Course: 1) Measurements of the ground state repopulation times of organic dyes will be made to determine the sensitivity of the spectrometer; 2) Application of the spectrometer to membrane dynamics and model heme proteins will be performed to study the role of these effects in cellular function and cooperativity.

Publications:

Smith, P.D., Liesegang, G.W.: Characteristics of a vidicon detector for 3-D spectroscopic applications. Biophys. J. 33, 186a, 1981.

Liesegang, G.W. and Smith, P.D.: Improving vidicon linearity in the pulsed illumination mode. Applied Optics. 20, 2640 (1981)

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10079-01

PERIOD COVERED

October 1, 1980 to September 30, 1980

TITLE OF PROJECT (80 characters or less)

Optical and Laser Engineering Support

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	P. Smith	Visiting Scientist	BEIB DRS
OTHERS:	R. Hendler	Section Chief	LB NHLBI
	M. Gottlieb		LPB NIAMDD
	R. Nakamura		LPP NIMH
	H. Cascio		BEIB DRS
	T. Clem		BEIB DRS
	R. Bonner		BEIB DRS

COOPERATING UNITS (if any)

LP, NHLBI; LPB-NIAMDD; LPP-NIMH

LAB/BRANCH

BEIB

SECTION

EEE

INSTITUTE AND LOCATION

NIH, DRS, Bethesda, Md. 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
0.7	0.35	0.2

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Optical support has been provided for the study of very small absorbance changes occurring in turbid cytochrome suspensions and for projection of transient images to measure animal and human response functions. Laser support has been provided for measurement of the phosphorescence resulting from laser excitation of dye molecules embedded in biological membranes. Substantial electronic support has been provided in all cases.

Objectives: To provide assistance in the optical and laser fields for collaborative efforts with investigators requiring this support.

Major Findings: A complete redesign of the light source and optical systems was necessary to reduce the noise in a commercial multi-channel spectrometer (RH). At full gain a peak to peak noise of 15mv is obtained which allows a baseline to be set corresponding to a specific redox state of a cytochrome suspension. By sequentially incrementing the base, full wavelength and time resolution of all the cytochrome redox states is thus obtained.

The shutter of a f1.9 75 mm recording lens was removed and replaced by a fast, electronically activated, two bladed shutter (RN). The modified lens assembly was mounted in a housing suitable for projection of a video CRT image onto a viewing screen. The completed assembly allows an image to be drawn on the CRT screen from computer memory after which the shutter is opened for varied times down to a minimum of 5 ms. A repetition rate of up to 10 frames per second is available.

A dye laser system, using coumarin 6, generating a 1 μ second, 1 Joule pulse at 531 nm has been provided (MG). This light stimulates the dye rosin embedded in a red cell membrane. A detection circuit has been constructed to monitor the resulting phosphorescence, from which the fluidity of the dye in the membrane can be determined. An important feature of the detection circuit is a dynode switching design which reduces the photomultiplier gain during the laser pulse.

Proposed Course: Further development of the red cell membrane experiment to improve the detection unit and to study the effect of various chemicals on membrane function.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10080-01

PERIOD COVERED
October 1, 1980 to September 30, 81

TITLE OF PROJECT (80 characters or less)
Multi-Element Array Detection

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	P. Smith	Visiting Scientist	BEIB DRS
OTHERS:	H. Cascio	Electronic Engineer	BEIB DRS
	I. Levin	Section Chief	LCP NIAMDD
	R. Balaban	Staff Fellow	KE NHLBI
	J. Hofrichter		LCP NIAMDD

COOPERATING UNITS (if any)
LCP NIAMDD; KENHLBI

LAB/BRANCH
BEIB

SECTION
EEE

INSTITUTE AND LOCATION
NIH, DRS, Bethesda, Md. 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
0.5	0.5	

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Multi-element array detectors are being interfaced to varied experimental arrangements to enable simultaneous detection of multiple events with a consequential reduction in experimental time. These projects are similar in nature and are in the initial states of development.

OBJECTIVES: To provide support and expertise in the interfacing of multi-element arrays as experimental detectors. These detectors are becoming increasingly applied, and it is expected the experience gained on these applications will be of use in future collaborations.

Methods Employed: The detectors for all applications are manufactured by Princeton Applied Research. In two cases, (RB, JH) the detectors are vidicon; in the third case, the detector is a multi-element diode array.

An electronic circuit was designed and constructed to allow the electron beam reading voltage to be switched after the completion of the preparation frames. This significantly improves the linearty of response of the vidicon under pulse illumination conditions; for a 1.5V increment in voltage a correlation of fit to a straight line of 0.99 is obtained for the vidicon response. This circuit has been incorporated in the 1252 vidicon (JH).

A model 1254 SIT vidicon is to be used as the detector in fluorescence microscopy (RB). This vidicon will be interfaced directly to a Digital Equipment Corporation MNC11 computer which will be used for control of the vidicon and for data gathering. An electronic circuit is being designed to provide a standard video signal from the 1254 suitable for presentation to commercial monitor sets and video tape recorders. A Spectra-Physics model 164 krypton laser has been aligned for excitation of the fluorescence.

A model 1452 linear diode array detector is to be interfaced as a detector for Raman studies (IL). In this instance, an intelligent controller, which will direct the setting of the experiment sample temperature in a pre-programmed sequence and will direct the date gathering by the diode array, has been designed and is being constructed.

Proposed Course: To finish the design and testing of the various circuits before incorporating them into the experimental apparatus for evaluation. To write the programming necessary for control of the detector and for data gathering. To provide support for future usage of multi-element arrays.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10081-01

PERIOD COVERED

October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)

Photo-Irradiation of Cancer Cells

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	P. Smith	Visiting Scientist	BEIB DRS
OTHERS:	P. Ebert	Research Chemist	VB NCI
	R. Bonner		BEIB DRS
	D. Tschudy	Senior Investigator	MET NCI
	J. Costa	Staff Physician	CNB NIMH

COOPERATING UNITS (if any)

VB-NCI;MET-NCI;CNB-NIMH

LAB/BRANCH

BEIB

SECTION

EEE

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, Md. 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
1.0	0.7	0.3

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

The effect of various wavelengths of light have been studied for the relative effectiveness in killing leukemic L1210 cancer cells incubated with hematoporphyrin. Investigations were also performed to determine the enhancement of this light effect after introduction of enhancers into the medium which stimulate hematoporphyrin uptake by the L1210 cells.

Z01 RS 10081-01 BEI

Objectives: To establish dose levels of the illuminating light required to produce various reductions in viable cell population: To determine the relative merits of enhancers which stimulate hematoporphyrin uptake by L1210 cells in photo induced killing.

Methods Employed: A lantern slide projector was modified to provide an illuminated 2" by 2" area suitable for exposing the flasks containing the L1210 cells. Provision was made for insertion of interference filters at specific wavelengths corresponding to absorption peaks for hematoporphyrin (397 nm, 531 nm, 566 nm, 621 nm, and 636 nm) and also for accommodating heat rejection filters. Exposure levels of the illuminating light were measured using a commercial (EG & G) radiometer. Typical levels are 3 mw/cm^2. Exposure times ranged from less than one minute to 30 minutes.

Major Findings: The in vitro studies performed have demonstrated that L1210 cells are killed by light if they are previously incubated in the presence of hematoporphyrin. Plots of leg cell count vs. time show a linear increase in time for the non-illuminated control and a fall in cell count for two days followed by subsequent growth in parallel with the control for the illuminated cells. For lethal doses of illumination this growth does not resume. The effectiveness of the killing was determined by measuring the ratio of the curves after resumption of growth. 636 nm has been found to be almost non-effective in killing L1210 cells, with 397 nm, 531 nm, and 621 nm being the most effective: experiments are underway to establish the relative effectiveness of these wavelengths for future in vivo work where other factors complicate the selection of the most effective wavelength. A quantitative measure of the enhancement attained with succinyl acetone, dibucaine, and chloraquine has not yet been made though it has been observed that these agents reduce the illumination period for equivalent killing.

Significance: Phototherapy is becoming a course of treatment for certain types of cancer. By establishing wavelength criteria and enhancing the light effect, improved photo-therapy will be made possible.

Proposed Course: To extend the in vitro studies to in vivo work. Initial studies will be performed on mice.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10082-01

PERIOD COVERED

October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)

Protein Sequencer Modification

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	R.J. Lutz	Chemical Engineer	BEIB DRS
OTHER:	E. Appella	Chief	LCB NCI
	J. Martin	Medical Equipment Repairer	BEIB DRS
	K. Yonaha	Guest Worker	DBBP BB

COOPERATING UNITS (if any)

LCB/NCI, DBBP/BB

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Chemical Engineering

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, Md. 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
1.0	.75	.25

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Proteins serve an incredible variety of biological functions which are determined indirectly by the amino acid sequence in the protein. The most effective single method for sequence determination is the degradation technique of Edman, which is performed by an automated instrument manufactured by Beckman. By a repetitive sequence of processes, amino acids are chemically cleaved one by one from the N-terminal end of a large protein or polypeptide. Recently, proteins of considerable interest are being isolated only in minute quantities, too small for accurate determination on available automated instruments. The goal of our project is to discover improvements to the present protein sequencing methodology that will allow for "microsequencing." The present emphasis is on improvements in the design of the automated sequencer. The three main features in the design that require improvements are (1) reagent and solvent delivery valve mechanism, (2) vacuum system, (3) automatic conversion of cleaved amino acid to a more stable phenylthiohydantoin derivative for analysis.

Objectives: To discover improvements to the present protein sequence methodology that will allow for "microsequencing." Three areas are involved in the overall improvement of the present Edman degradation method: (1) sample purification and preparation, (2) reagent and solvent purification, (3) more sensitive analytical techniques, and (4) modification in the design of the automated sequencer. Ultimately, new approaches will be investigated for microsequencing of proteins such as solid phase, gas phase, and membrane reaction and separation techniques.

Methods Employed: The present emphasis is on modifications to the Beckman sequencer in three specific areas. (1) Reagent and Solvent Delivery Valves: A new, more reliable and precise valve has been designed for delivery of solvents and reagents to the reaction chamber (spinning cup). It is a specially designed manifold system with zero hold-up volume. All parts in contact with chemicals are made of teflon and therefore are inert. The new valve replaces a cumbersome system of valves in the old machine. (2) Vacuum System: High and low vacuum are regulated by two Leybold-Heraus stainless steel vacuum valves connected in series. These valves are connected to a rotary vane vacuum pump through a liquid nitrogen cold trap that allows vacuum down to 1 micron thus reducing backflux into the reactor of vapors from volatile solvents or reagents between run cycles. Vacuum pump oil stays cleaner longer. (3) Reaction Chamber: The reaction chamber has been redesigned to contain fewer O-ring seals thus reducing leakages of oxygen into the system which is detrimental to the chemical reaction scheme. (4) Automatic Converter: An automatic converter has been installed on the sequencer. This all glass unit converts the cleaved anilinothiazolinone amino acid derivatives to a more stable phenylthiohydantoin for eventual analysis and identification by high pressure liquid chromotography.

Significance: Proteins of significant scientific interest are often available only in sub-nanomole quantities. Progress in the elucidation of the primary structure of these proteins can be achieved by a number of improvements in techniques for amino acid sequence analysis. The first advances are being made now by employing technical improvements of the Beckman liquid-phase sequencer, including addition of an automated conversion device. New techniques now being tested may further improve protein sequence methodology, e.g. gas-phase instruments.

Proposed Course: (1) install new delivery valve unit on old Beckman 890C; (2) install new autoconverter; (3) incorporate improved vacuum system with liquid N_2 cold trap in system; (4) test assembled unit on standard protein (myoglobin); (5) check for lower limit of sensitivity of new unit (down to 1 nanomole sample); (6) consider improved design for solid-phase sequencing system; (7) study any new, proposed methods of sequence analysis.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10083-01

PERIOD COVERED

August 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)

Study of Oxygen Transport in Peruvian High Altitude Natives

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	C.C. Gibson	Electrical Engineer	BEIB,DRS
OTHER:	R.M. Winslow	M.D.	CDC
	H.G. Klein	M.D.	Bloodbank, CC
	S. Rosen		Bloodbank, CC
	N. Statham		CDC
	C.M. Monge	M.D.	U. Cayetano Heredia Lima, Peru
	E. Monge	M.D.	U. Cayetano Heredia Lima Peru

COOPERATING UNITS (if any)

lood Bank, Clinical Center Center for Disease Control, Atlanta, Georgia

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Electrical and Electronic Engineering Section

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
1.5	1.0	0.5

CHECK APPROPRIATE BOX(ES)

☒ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☒ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

A field trip to determine the work capacity of high altitude natives (14,850 ft) suffering from Monge's disease before and after phlebotomy. Using a computer controlled exercise stress test, several high altitude natives were tested before and after massive phlebotomy. Enough red cells were removed and replaced with albumin to lower their hemocrit to 50-52%. This usually meant that three liters of red cells were removed. In all cases, the improvement in performance was dramatic ranging from 50%-150% increase in work output.

Objectives: To see whether or not massive phlebotomy is of benefit to the high altitude native suffering from Monge's disease.

Methods: A breath by breath computer controlled exercise test was used, coupled with various opti-sats and catheters in place to measure arterial and veinous oxygen saturation. A Heamonetics cell separator was used for the phlebotomy.

Significance: Phlebotomized natives could work harder and longer than they could before. If this method works over a long period of time it will benefit the Peruvian people and economy directly.

Proposed Course: Another trip is planned for January 1982 to study the previous patients again, and to phlebotomize another series of patients, looking carefully at renal function and measuring red cell mass.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10084-01

PERIOD COVERED

October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)

Instrumentation for Microcalorimetry Data Acquisition and Correction

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	C.C. Gibson	Electronics Engineer	BEIB, DRS
OTHER:	R. L. Berger	Physicist	LTD, NHLBI
	C. Mudd	Mechanical Engineer	BEIB, DRS

COOPERATING UNITS (if any)

Laboratory for Technical Development, NHLBI

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Electrical and Engineering Section

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
2.0	2.0	0

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

A microcomputer based data collection and reduction system has been implemented to calculate the total heat output and power vs. time of a batch calorimeter with provisions for plotting the data.

PHS-6040
(Rev. 2-81)

Objectives: To provide a data collection system capable of correcting the input data so that a true heat of reaction and power curve can be realized from a batch calorimeter.

Methods: A programmable gain 16 bit A/D converter has been utilized to obtain the needed accuracy for a finite element scheme to do the data correction.

Significance: The data collection and reduction scheme allows detection of 5×10^{-9} calories for enzyme reactions thus allowing many more reactions to be studied.

Proposed Course: To average the incoming data and extend the system to include a differential-ph-thermal titration apparatus.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10085-01

PERIOD COVERED

July 26, 1981 to September 30, 1981

TITLE OF PROJECT (80 characters or less)

Buckling Modes of Growing Venules

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI: A.M. Waxman	Physical Scientist	BEIB, DRS

COOPERATING UNITS (if any)

None

LAB/BRANCH

iomedical Engineering and Instrumentation Branch

SECTION

Mechanical Engineering

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
0.05	0.05	0.00

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

A physical model has been developed to describe the mechanics of growing blood vessels. The blood vessel is treated as a growing elastic shell imbedded in a surrounding viscous fluid (the tissue). As the vessel grows, it buckles in any of three possible modes, varicose, sinuous, or helical, and with a particular wavelength in each case. Solutions of the governing equations for the geometry and mechanical force balance are currently being sought for the sinuous and helical modes. This work is an extension of previous work on the axisymmetric, varicose mode.

Objectives: The short term objective is to develop confidence in the conceptual model proposed here for the stimulated growth of small blood vessels. Satisfactory comparison between theoretically predicted wavelengths for the various buckling modes with measurements made from experiments on tumor angiogenesis would lend credence to the ideas set forth in earlier work.

Methods Employed: Analytical methods are used to solve the equations governing the physical model. The nonlinear partial differential equations are solved exactly for the case of a uniformly dilating vessel. The buckling sets in as an instability of the slowly dilating state. The dominant wavelengths are extrated by a perturbation analysis for each separate mode.

Significance: With regard to tumor angiogenesis, the model gives us a framework which helps explain the presence of tortuous and focally dilated blood vessels in the vicinity of a tumor inplant. It seems that new capillaries sprout in the vicinity of the wavecrests associated with buckling and thus, the buckling of preexisting vessels is intimately related to the vascularization process of the tumor itself.

Proposed Course: If the buckling theory continues to yield satisfactory predictions for the wavelengths of the various modes, it can then be utilized to explore the sprouting phenomenon. By considering the reaction-diffusion dynamics of growth promoters and inhibitors on buckled surfaces, we hope to identify sprouting sites as regions of enhanced promoter concentration on the vessel surface.

Publications:

Waxman, A.M.: Blood vessel growth as a problem in morphogenesis - A physical theory. Microvascular Research (in press).

Waxman, A.M.: A continuum approach to blood vessel growth-axisymmetric elastic structures. J. Theoretical Biology (in press).

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10086-01

PERIOD COVERED

July 26, 1981 to September 30, 1981

TITLE OF PROJECT (80 characters or less)

Theory of Lateral Diffusion in Cell Membranes

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI: A.M. Waxman	Physical Scientist	BEIB, DRS

COOPERATING UNITS (if any)

None

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Mechanical Engineering

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
0.05	0.05	0.00

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Lateral diffusion of proteins in cell membranes is treated as a problem in Brownian motion through a two-dimensional viscous fluid membrane with curvature and of finite area. Analogous to the Stokes-Einstein relation for diffusion through a viscous bulk fluid, we seek to relate the diffusion constant of a protein in a membrane to the rheological and geometrical properties of the membrane as well as to the size of the protein molecule.

Objectives: Our first objective is to calculate the hydrodynamic drag force exerted on a protein moving through a fluid membrane of finite area which possesses finite curvature as well. This drag force may then be utilized in a Langevin-type approach to Brownian motion in such a membrane.

Significance: We hope to develop a physical understanding of lateral diffusion in cell membranes. Diseased states of the membrane will affect its rheology as well as its shape, and this should reflect itself in altered diffusion rates of proteins. This, in turn, will influence the overall performance of the cell.

Proposed Course: At first, the membrane is being treated as a two-dimensional viscous fluid. In the future we hope to consider more realistic viscoelatic fluid models for the cell membrane.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10087-01

PERIOD COVERED

July 26, 1981 to September 30, 1981

TITLE OF PROJECT (80 characters or less)

Mechanics of Red Blood Cells in Flow

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	A.M. Waxman	Physical Scientist	BEIB, DRS

COOPERATING UNITS (if any)

None

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Mechanical Engineering

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, Md. 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
0.1	0.1	0.0

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

The red blood cell is modeled as a fluid droplet surrounded by a viscoelastic fluid membrane which possesses a bending resistance. The resting shape of the cell is taken to be a biconcave disk. When the cell is immersed in a shear flow, it deforms in shape and sets up an internal circulation as well as a membrane flow. We seek to calculate such shapes from mechanical considerations, and relate shape and flow to membrane rheology.

Objectives: We seek to relate red cell shape and deformability to membrane rheology via these hydrodynamic calculations. Then, by comparing the calculated shapes to those observed experimentally, we hope to determine the rheological constants which characterize the mechanical properties of the lipid bilayer-spectrin composite which forms the membrane.

Methods Employed: The formalism developed by Waxman to describe the mechanics of deforming surface continua shall be utilized here. This theory of the kinematics, dynamics, and rheology of evolving surface phases enables us to describe the membrane flow for a deforming cell. The internal flow shall be modeled as an incompressible viscous fluid. The governing equations must be solved numerically.

Significance: Various diseases states are characterized by altered mechanical properties of the erythrocyte membrane. This manifests itself in altered deformability, and this in turn affects the flow properties of blood (as a suspension of red cells). Thus, it is important to understand the mechanics of the membrane itself and how it relates to red cell deformability.

Publications:

Waxman, A.M.: Dynamics of a couple-stress fluid membrane. J. Fluid Mechanics (in press).

Waxman, A.M.: A corotational time-derivative for surface tensors, constitutive relations, and a new measure of bending strain. J. Non-Newtonian Fluid Mechanics (in press).

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10088-01

PERIOD COVERED

October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)

Multimode R5232-C Data Switch

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI: C.C. Gibson	Electrical Engineer	BEIB, DRS

COOPERATING UNITS (if any)

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Electrical and Electronic Engineering Section

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, Md. 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
0.2	0.1	0.1

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

With the advent of smart instrumentation, methods are needed to transfer the data from the instrument to a large computer for analysis. This particular device allows a large coulter counter to transfer its data to either an NIH 7000 terminal or to the DEC-10 computer without cable switching.

Objective: To transfer data from a coulter counter to the DEC-10 computer.

Methods: This switch utilizes a diode OR-Gate so that an interactive terminal can stay on line to the computer at the same time the Coulter counter is on line and transfering data.

Significance: This device enabled the researcher to process twice as many samples per day.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10089-01

PERIOD COVERED
October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)

Non-invasive Hemoglobin Measurement

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	C.C. Gibson	Electronics Engineer	BEIB, DRS
OTHER:	H.G. Klein	M.D.	Blood Bank, C.C.
	S. Rosen		Blood Bank, C.C.
	V. Weber	R.N.	Blood Bank, C.C.

COOPERATING UNITS (if any)

Blood Bank. Clinical Center

LAB/BRANCH
Biomedical Engineering and Instrumentation .

SECTION
Electrical and Electronic Engineering Section

INSTITUTE AND LOCATION
DRS, NIH, Bethesda, Md. 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
1.0	0.4	0.6

CHECK APPROPRIATE BOX(ES)

☒ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

In the treatment of thalassemia, iron poisoning from frequent transfusions is the primary cause of death. If neocytes only are transfused then the frequency of transfusions is cut by half. To collect neocytes, a method was needed to continuously monitor the hemoglobin concentration of the output of an IBM continuous flow cell separator. A device was designed and built that continuously measures hemoglobin concentration non-invasively. The sensor head fits over the output tube and uses optical methods to measure the hemoglobin concentration. The device will measure from 0-12g% concentration with less than .3g% error.

Objectives: To measure hemoglobin concentration from 1.g% to 5.0g% non-invasively and continuously.

Methods Used: Optical density measurements are done using optical feedback through the solution being measured. The device is slipped over the output tube of the IBM continuous flow cell separator making it completely non-invasive.

Significance: This device aids in the collection of neocytes and allows the operator of the cell separator to keep the interface essentially constant.

Proposed Course: To more fully calibrate the instrument and prepare a publication.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10090-01

PERIOD COVERED
October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)

Computer-controlled Fermentation System

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	T.R. Clem, Sr.	Electronic Engineer	EEES,BEIB, DRS
OTHER:	Yossi Shiloach	Chief, Power Plant Unit	LNE NIADDK

COOPERATING UNITS (if any)
LNE, NIADDK

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Electrical and Electronic Engineering

INSTITUTE AND LOCATION
DRS, NIH, Bethesda, Md. 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
0.3	0.2	0.1

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

A computer controlled fermentation system is being developed for monitoring and controlling the fermentation process. The system will be assembled using primarily commercial instruments interconnected via the IEEE-488 GPIB. This approach will allow scaling the process to different size vats with a minimum of changes required.

Z01 RS 10090-01 BEI

Objectives: Design and implement an instrumentation and control system to allow monitoring and control of the fermentation process in any of several fermentation vats.

Methods Employed: The first system to be assembled will consist of some instruments which were already in use in the pilot plant and some instruments which were purchased specifically for this project, all connected to an inexpensive desk-top computer. The computer is programmible in BASIC, which allows the experimenter to easily produce the controlling and monitoring programs. Most all interconnections to the computer will be via the IEEE-488 GPIB.

Significance: Computer monitoring and controlling of the fermentation process will produce several significant advantages over the present methods. By using the computer to make decisions based on what is occuring in the fermentation process, parameters can automatically be altered to produce either an increased yield of a desired product or a more pure form of the product. The computer can also perform some of the "housekeeping" tasks associated with running a fermentation process that would normally require an operator.

Proposed Course: To assemble a basic system to begin controlling and monitoring a fermentation process to determine where further effort or refinement is necessary.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10091-01

PERIOD COVERED

October 1, 1980 to September 31, 1981

TITLE OF PROJECT (80 characters or less)

Mechanics of Red Blood Cell Membrane

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI: D.R. Markle	Biomedical Engineer	BEIB, DRS

COOPERATING UNITS (if any)

LAB/BRANCH

Biomedical Engineering and Instrumentation Branch

SECTION

Mechanical Engineering

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, Md. 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
.1	.1	

CHECK APPROPRIATE BOX(ES)

☒ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

a micromanipulation system consisting of an inverted microscope, two micro manipulators and video equipment necessary for the recording and analysis of data has recently been acquired. This system will be used to investigate the intrinsic material properties of red cell membrane and large lipid vesicles using micropipette aspiration and flow channel techniques.

Methods: Presently both micropipette aspiration and slow channel techniques are being developed and will be used in the above studies. However, the system is flexible and can be readily adopted to the needs of any specific experiment.

Proposed Course: Initially the system will be used to investigate the intrinsic material properties of red cell membrane in diseased states. At the present time red blood cells obtained from diabetics are of primary interest. However, red cells from patients with sickle cell anemia and muscular dystrophy etc. are also of interest and will be studied. Other uses of this system may include studies of cell lysis during the freezing and thawing process used in blood storage, measurement of the affinity of red blood cell membranes for particle surfaces, and measurements of the mechanical properties of both pure and multiphase vesicle systems.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10092-01

PERIOD COVERED

October 1, 1980 to September 30, 1981

TITLE OF PROJECT (30 characters or less)

Low Duty Cycle, Pulsed Electromagnetic Blood Flowmeter

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	C.P. Mudd	Biomedical Engineer	MES, BEIB, DRS
	R. Patterson	Senior Investigator	Cardiology, NHLBI

COOPERATING UNITS (if any)

Cardiology Branch, NHLBI

LAB/BRANCH

BEIB

SECTION

MES

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, Md. 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
0.2	0.2	

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

To design, construct, and evaluate a prototype of a low duty cycle pulsed electromagnetic blood flometer. The design will use an excitation scheme which will simplify probe construction and also increase reliability.

Z01 RS 10092-01 BEI

Objective: By using a pulsed excitation scheme, it is possible to eliminate the quadrature voltage problem. Without the quadrature signal, we can simplify the probe design and thus produce a more reliable instrument.

Significance: If we use A.C. excitation in an electromagnetic flowmeter, a quadrature voltage, E_q is created which is generally orders of magnitude greater in amplitude than the flow-induced signal. In practice, to reduce E_q, the probes are partially assembled and when excited, the electrode leads are moved to reduce E_q. The probes are then encapsulated. Because of this procedure, the probe cost is high, $500/unit, and any subsequent change in the capacitive or inductive voltages will upset the nulled condition and increase E_q thus rendering the probe useless. If the above scheme can be implemented, this problem will be eliminated.

Proposed Course: (1) Design the signal amplifier and associated circuits; (2) Design a pulse amplifier to drive the probes; (3) Redesign the probe to ensure that the magnetic field is constant across the lumen.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
NOTICE OF
INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 RS 10094-01

PERIOD COVERED
October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)
Removal of Atherosclerotic Plaque from Arterial Walls Using A Special Purpose Catheter

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	S.R. Goldstein	Chief	MES BEIB DRS
OTHER:	K. Kent	Chief	CDS CB NHLBI

COOPERATING UNITS (if any)
Cardiovascular Diagnosis Section, Cardiology Branch, NHLBI

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Mechanical Engineering

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

A variety of concepts will be investigated to determine the feasibility of developing a special purpose catheter to removed arterial plaque from coronary vessels. Use of lasers, ultrasonics, and mechanical means will be evaluated as appropriate.

Objective: To conceive and determine the feasibility of various techniques of removal of plaque from arterial wall.

Significance: The development of a technique for removal of plaque via a catheter would aleviate the need for open chest surgery in some cases, and allow treatment in other cases where such surgery cannot be done. This would be of great importance in the treatment of coronary artery disease.

Proposed Course: a) Conceive of and evaluate concepts for plaque removal; where appropriate perform critical experiments, b) develop a miniature fiber optic imaging catheter to visually examine coronary vessels.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10095-01 BEI

PERIOD COVERED
October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)

Multiple Probe pH Measurement System for Canine Myocardium

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	D. Markle	Biomedical Engineer	MES BEIB DRS
OTHER:	D. McGuire	Mathematician	MES BEIB DRS
	S. Goldstein	Chief	MES BEIB DRS
	R. Patterson	Senior Investigator	NHLBI

COOPERATING UNITS (if any)
Cardiology Branch, NHLBI

LAB/BRANCH
Biomedical Enginering and Instrumentation

SECTION
Mechanical Engineering

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
1.5	1.5	

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

For the past several years, considerable effort has been expended on the development of a miniature fiber optic pH probe for physiological use. With the first generation of probes and support equipment the feasibility of optically measuring pH via a pH sensitive dye was demonstrated and many subtleties associated with the probe construction and use made apparent. With this knowledge and experience and improved probe and multichannel support system has been designed and constructed and is presently being used to measure pH in the wall of beating canine hearts.

Objectives: To provide a pH probe which was rugged, easily and atriumatically inserted into a beating heart, free from motion artifacts, quick to respond to pH changes and able to resolve pH with a spatial resolution of approximately 0.5mm. Furthermore the support system was required to provide continuous data (visual and hard copy) for each of five probes.

Methods Employed: The probe was redesigned to fit into a 25 gauge (0.5mm diameter) stainless steel needle by reducing the diameters of the optical fibers to 0.075mm and the inside diameter of the semi-permeable membrane is provided by two slots machined in the needle wall and a transverse hole 0.368 mm in diameter. This design increased the probes' durability and eliminated all motion artifacts. In addition, the smaller probe dimensions reduced the insertion trauma and decreased the 90% step-response time from approximately 90 to 30 seconds. The spatial resolution of the probe was increased by concurrently reducing the dye column length to 0.12 mm and terminating the column with a reflective surface. The mirror surface is required to avoid excessive light loss through the end of the dye column.

Significance: At the present time this is the only system available to measure tissue pH in-vivo and on line. Such information is of use to experimental cardiologists interested in evaluating drugs which affect tissue perfusion, obstetricians interested in monitoring fetal scalp pH and biomedical researchers in general.

Proposed Course: To further improve the reliability and ease of operation of the system and to reduce its size and cost.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10096-01

PERIOD COVERED
October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)

Light Scattering Method for Evaluation of Platelets

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	R.F. Bonner	Physicist	BEIB DRS
OTHER:	P. Smith	Visiting Scientist	BEIB DRS
	J. Fratantoni	Dir. Blood Bank Products	BB FDA
	B. Poindexter	Biologist	BB FDA

COOPERATING UNITS (if any)
Bureau of Biologics, FDA

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Electrical and Electronic Engineering

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Assessment of the functional status of platelets for transfusion is confounded by the inherent complexity of the cell, as well as the intricate requirements of sample preparation. A correlation between discoid shape and functional integrity of the platelet has been established. We have developed a simple prototype instrument for measuring the fraction of discoid platelets quantitatively in standard blood bank platelet concentrate units within their bags. Our instrument detects the light scattered (633nm) between 5 and 6 degrees of the forward beam. The plasma may be made to flow perpendicular to the incident beam through a narrow parallel plate gap. Discs orient face on to the beam and consequently scatter light through a smaller angle than the randomly oriented platelet. The change in light scattered at 5 degrees for the flowing (oriented) platelets from that of resting (randomly oriented) platelets is a quantitative measure of the fraction of discoid platelets. This measurement has been correlated with other measures of platelet function.

Rigorous light scattering theory has been applied to this problem in order to provide a quantitiative method for the wide range of blood bank samples.

Objectives: Develop an optical method to evaluate platelets in standard blood bank platelet concentrates.

Methods: Angular light scattering studies on platelet suspensions and from blood bank samples in PVC bags formed the basis of a prototype low-angle light scattering instrument. Measurement on a large number of platelet concentrates in parallel with biochemical and visual grading provided a basis for the evaluation of the light scattering method. Light scattering theory is being applied to this data base in order to understand the effects of the platelet number density and fraction that are discs on the measured values. This theoretical understanding will direct modifications of the instrument in order to provide best quantitative assessment for the wide range of platelet concentrates produced by blood banks.

Major Findings: The difference in scattering at 5 degrees between oriented and unoriented platelet suspensions provides a quantitative assessment of platelet function as determined by parallel methods. The prototype instrument allows the rapid (1 minute) assessment directly on the platelet concentrate bag without the possibility of contamination.

Multiple scattering theory predicts the observed dependence on platelet number density and sample thickness and indicates that a 5 degree measurement for a 3mm sample path is optimum for the observed range of platelet densities (0.6 to $2.0 \cdot 10^6$ per mm^3).

The relaxation rate of platelet orientation also provides a measure of platelet asymmetry, which however, is strongly dependent on the normal variations in plasma viscosity.

Significance: A rapid, noninvasive quantitative optical grading of platelet concentrates would provide optimal utilization of the blood bank product for transfusion. Additionally it would allow continuous quality control of the preparation and storage of the platelet concentrates at blood banks and hospitals.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10097-01

PERIOD COVERED
October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)
Mechanics of the Left Ventricle

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	R.S. Chadwick	Biomedical Engineer	BEIB DRS
OTHER:	R. Patterson	Senior Investigator	Cardiology NHLBI

COOPERATING UNITS (if any)
NHLBI-Cardiology Branch

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Mechanical Engineering

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, Md. 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

A theoretical analysis of the mechanics of the left ventricle has been undertaken in which the myocardium is modeled as a fluid-fiber continuum. The passive and active length-tension relations of papillary muscle are applied to the three-dimensional architecture of the myocardium. The anisotropic elastic behavior is crucial to understanding the contractility of the myocardium, the development of systolic pressure, pumping of blood out of the ventricular chamber, and the flow of blood in the myocardium itself.

Z01 RS 10097-01 BEI

Objectives: To develop a quantitative theory which describes the mechanical events in the left ventricle throughout the cardiac cycle.

Methods Employed: The myocardium is idealized as a continuum of muscle fibers imbedded in an incompressible fluid. The fiber direction field measured by Streeter is an essential part of the theory in which a pressure field develops in the tissue to support the tensile streses which act along the fiber directions. The passive and active states of the muscle fibers are characterized by the known tension-sarcomere length relations for papillary muscle. Boundary value problems are formulated for the various phases of the cardiac cycle.

Major Findings: Solutions have been obtained so far for the passive diastolic filling phase and then subsequent isovolumic contraction in a finite cylindrical model of the left ventricle. Some interesting results already emerge from the analyses, e.g. the isometric contraction in a muscle preparation is not equivalent to the isovolumic contraction phase of the heart. Also the physiological distribution of fiber angles appears to maximize the development of systolic pressure.

Significance: Further development of the theory will help in the understanding of ventricular hypertrophy, and help to quantify contractility which is an important index in the assessment myocardial ischemia.

Proposed Course: The analysis will be extended to complete the cardiac cycle, a more realistic ventricular geometry will be considered, and an analysis of myocardial blood flow will be undertaken.

Publications:

Chadwick, R.S.: The Myocardium as a Fluid-Fiber Continuum: Passive Equilibrium Configuration. 1981 Advances in Bioengineering, ASME, (in press).

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10098-01

PERIOD COVERED

October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)

CO_2 Laser Vitrectomy

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	S.B. Leighton	MES BEIB DRS
	R. Bonner	EEES BEIB DRS
OTHER:	S. Meyers	NEI

COOPERATING UNITS (if any)

MES, EEES

LAB/BRANCH

BEIB

SECTION

MES

INSTITUTE AND LOCATION

NIH, Bethesda, Md. 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
.45	.4	.05

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

A pulsed CO_2 laser vitrectomy system is being developed for NEI. It is expected that the pulsed laser energy will locally cut vitreous bands without creating transient tension on their vertical attachments. Additionally the infrared pulse will be absorbed within 100 μm of the intraocular probe without appreciable thermal diffusion (allowing access to bands lying 1-2 mm above the retina). The laser has been set up and tested in an animal surgery room. An articulated arm and waveguide intraocular probe are being constructed. An alternate fiber optic delivery system supplied by a commercial source is being tested.

Objective: To develop an intraocular CO_2 laser surgical instrument capable of cutting vitreous bands without damage to nearby retina.

Methods Employed: Construction of the laser system and testing it on living animals with vitreous bands (rabbits, monkeys). Construction to date includes adaptation of commercial CO_2 laser to two prototype delivery systems: 1) articulated arm with protected silver mirrors and lens containing tapered gold surface waveguide (1mm diameter for intraocular tip) with diamond window; 2) thallium bromoiodide fiber optic delivery system. Animal experiments to date suggest laser system with $\geq$ 25% efficiency probe (fiber optic) are sufficient to cut vitreous bands without short term retinal damage at $>$ 2mm from probe. The relative efficacy of the two prototype delivery systems will be further tested. Testing of components of prototype 1) articulated arm system suggest an efficiency of $>$25% when a focusing lens is used.

Significance: The present laser system with one or the other delivery system appears to offer a viable alternative to current mechanical vitrectomy cutters.

Proposed Course: Further animal testing of the requirements, methodology, and hazards of the laser vitrectomy cutter are being pursued. Accompanying modification of two prototype delivery systems will provide the vitreous surgeon with the most versatile and useful instrument for evaluation of efficacy in clinical trials.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10099-01 BEI

PERIOD COVERED
October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)
Cochlear Mechanics

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI: R. S. Chadwick Biomedical Engineer BEIB DRS

COOPERATING UNITS (if any)

LAB/BRANCH
Biomedical Engineering and Instrumentation Branch

SECTION
Mechanical Engineering

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
0.2	0.2	

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

This study is concerned with a theoretical analysis of the propagation of mechanical waves in the cochlea. These waves result from the input action of the stapes footplate and the subsequent interaction of the basilar membrane with the cochlear fluids. The stereocilia of the hair cells deform due to the wave motion and convert information contained in the waveform to electrical impulses. A quantitative understanding of the wave patterns and the mechanical factors affecting them is essential for an understanding of the hearing process. The influence of cochlear geometry, fluid and membrane viscosity, and elastic coupling in the basilar membrane are being studied.

Objectives: To calculate the velocity and pressure fields in the cochlear fluids, and the displacement field of the basilar membrane, in response to various types of physiological input sounds.

Methods Employed: The appropriate equations of fluid and solid mechanics are written in linearized form to obtain the basic hydroelastic boundary value problem. This problem is then solved using a variety of methods of asymptotic analysis. The basic small parameter is the slenderness of the cochlear geometry. Low and high frequency limits are studies, as well as the effects of elastic anisotrophy of the basilar membrane.

Significance: The ear has the ability to distinguish different tones with high sensitivity. One outstanding question in auditory physiology is whether the main auditory analysis is performed mechanically or by neural means. Theoretical calculations of the type being done in ths project will help to answer this question.

Proposed Course: A study of the micromechanics of Organ of Corti is planned, as well as the electro-mechanics of the hair cell transduction process.

Publications:

Chadwick, R.S.: Studies in Cochlear Mechanics. Lecture Notes in Biomathematics, in Proceedings of NSF-CBMS Regional Conference on Mathematical Modeling of the Hearing Process 1980, Springer-Verlag, NY, in press.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10100-01 BEI

PERIOD COVERED
October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)
Mechanics of Muscle Contraction

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	R. S. Chadwick	Biomedical Engineer	BEIB DRS
OTHER:	R.J. Podolsky	Chief	LPB NIAMDD

COOPERATING UNITS (if any)
NIAMDD - Laboratory of Physical Biology

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Mechanical Engineering

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
0.3	0.	

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

An outstanding unanswered question in muscle physiology is concerned with the details of the molecular mechanisms involved in the generation of force. Physiological experiments on striated muscle aimed at obtaining information at the cross bridge level are often complicated by unwanted effects which make interpretation difficult. Some of these are nonuniform sarcomere lengths, end effects due to tendons and clamping, dispersion of fiber lengths, nonalignment of striations across the muscle cross section, and mechanical wave propagation effects. A continuum theory incorporating sarcomere interactions would be very useful in interpreting physiological data.

Objectives: To develop a continuum theory of striated muscle contraction incorporating sarcomere interactions for the resting, active, and rigor physiological states.

Methods Employed: As a first step, a one-dimensional theory will be developed which will incorporate the three distinct length scales which appear in the mechanical descirption of muscle contraction. Events at the cross bridge level occur on a scale of nanometers, those at the sarcomere level occur on a scale of microns, while the total length of the fiber is typically several millimeters. A fiber is composed of about 10^4 sarcomeres in series. The equations of motion and energy of a sarcomere involve the statistical mechanics and biochemistry of the cross bridge interactions and the interactions with nearest neighbor sarcomeres. The continuum limit of the equations of the chain yields a system of partial differential equations to be studied.

Significance: Mathematical solutions of the boundary value problems can simulate and lead to a better understanding of physiological experiments on muscle contraction.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10101-01 BEI

PERIOD COVERED
October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)
Cryopreservation of Neural Tissue

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	R.L.Levin	Mechanical Engineer	BEIB DRS
OTHER:	D.C.Klein	Senior Investigator	LDN NICHHD

COOPERATING UNITS (if any)
LDN-MICHHD

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Mechanical Engineering

INSTITUTE AND LOCATION
DRS, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
0.02		

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

The purpose of this project is to develop an optimum freeze-thaw protocol for neural tissue in order to permit its long term preservation.

PHS-6040
(Rev. 2-81)

Objectives: To develop optimum techniques for the long term cryopreservation of neural tissue.

Methods Employed: An experimental study of the response of neural tissue to freezing and thawing at specific rates will be conducted utilizing a controlled rate LN_2-microwave freeze-thaw device previously developed.

Significance: The long term cryopreservation of neural tissue will greatly facilitate analyses of neurological activity and the development of neural tissue transplant techniques.

Proposed Course: A comprehensive experimental study of the optimum cryopreservation protocol for neural tissue will be investigated using a controlled-rate LN_2-microwave freeze-thaw device.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10102-01 BEI

PERIOD COVERED
October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)
Osmotic Behavior of Perfused Tissues and Organs

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	R.L.Levin	Mechanical Engineer	BEIB DRS

COOPERATING UNITS (if any)

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Mechanical Engineering

INSTITUTE AND LOCATION
DRS, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
0.15		

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

The purpose of this project is to study the osmotic behavior of perfused tissues and organs during the introduction and removal of cryoprotective agents (CPAs) from both an analytical and an experimental point of view. Comparison of theoretical predictions of organ behavior during CPA introduction and removal based upon a newly developed non steady state mass transfer model with experimental observations of the responses of perfused organs to changes in the composition of their perfusates will hopefully facilitate the development of optimum CPA introduction and removal protocols.

Objectives:

(1) To develop a non-steady state mass transfer model of the osmotic response of perfused tissue and organs to the introduction and removal of cryoprotective agents experimentally.

(2) To experimentally observe the osmotic response (i.e., changes in weight, vascular resistance and effluent composition) of isolated perfused organs to the introduction and removal of cryoprotective agents.

(3) To correlate our analytical and experimental findings and deduce the rate-limiting transport parameters.

(4) To develop optimum CPA introduction/removal protocols.

Methods Employed:

(1) Mathematical modeling and data analysis will be accomplished through the use of NIH's DEC-10 computing system and associated computer graphics facility.

(2) Experimental observations will be conducted with the aid of a microprocessor controlled organ perfusion system.

Significance: High concentrations of cryoprotective agents (CPAs) such as glycerol and dimethylsulfoxide are necessary for the successful cryopreservation of cells, tissues, and organs. Unfortunately, the introduction of CPAs prior to freezing and their removal after thawing has been documented in many instances to be as damaging as the freeze-thaw process itself. In order to help avoid the possible adverse osmotic effects observed by many investigators during CPA introduction and removal, a comprehensive theoretical and experimental analysis of the osmotic behavior of perfused tissue and organs is necessary.

Major Findings: Comparison of our preliminary theoretical and experimental results shows a large degree of both qualitative and quantitative agreement for the overall osmotic behavior of a perfused organ. Specifically, in both instances, a lack of high molecular solute in the perfusate seems to cause a significant gain in weight. Furthermore, our results seem to indicate that the initial weight gain during CPA removal is much greater than the initial weight loss and subsequent weight gain during CPA introduction. These similarities suggest that our work should provide some indications as to the nature of the osmotic stresses and strains which might result in tissue or organ damage during CPA introduction/removal and therefore facilitate the development of optimum CPA introduction/removal protocols.

Proposed Course: To continue our current theoretical and experimental studies of the responses of perfused organs to the introduction and removal of cryoprotective agents.

Collaborator: The experimental aspects of this project are being conducted in the laboratories of Dr. David E. Pegg, Chief of the MRC Medical Cryobiology Group, Cambridge University Department of Surgery, Cambridge, England.

Publications:

Levin, R.L.: Osmotic Effects of Introducing and Removing Cryoprotectants: Perfused Tissue and Organs". Adv. BioEngineering. (In press).

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10103-01

PERIOD COVERED

October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)

Triple Laser - Multi Parameter Flow Cytometry System for Study of Tumor Cell Kinetics

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	W.H. Schuette	Chief	ACES BEIB DRS
	S.E. Shackney	Acting Chief	CKS CPB DCT NCI
OTHER:	C.A. Smith	Med. Tech.	CKS CPB DCT NCI
	S.J. Occhipinti	Micro Biol.	CKS CPB DCT NCI
	H. Mujagic	Visiting Scientist	CKS CPB DCT NCI
	S.S. Chen	Visiting Fellow	CKS CPB DCT NCI

COOPERATING UNITS (if any)

DRS - NCI

LAB/BRANCH

DRS-BEIB

SECTION

ACES

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, Md. 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
3	2	1

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

A triple laser flow cytometry system is being developed so that various imuno-fluorescent labeling techniques may be employed for the investigation of tumor cell kinetics. Three laser beams at different wave lengths will be made to intersect a tumor cell flow stream passing through a quartz cuvette so that multi-parameter signals may be obtained. These signals will be processed by specialized electronics and then analyzed by means of a PDP 11 computer.

Publications:

Shackney, S.E., Schuette, W.H., Smith, C.A., Nichols, P.W. and Lukes, R.J.: Patterns of Cell Proliferation in Relation to Aneuploidy by Flow Cytometry in the Non-Hodgkin's Lymphomas. In Proc. of 17th Annual Mtg. of the American Society of Clinical Oncology, Vol. 22, P337 April 1981

Levine, A., Shackney, S.E., Cunningham, R.E., Smith, C.A. Schuette, W.H., Teitelbaum, A.H., Nichols, P.W., Stolinsky, P.C., and Lukes, R.J.: Therapeutic Response and Survival in B and T Cell Lymphomas (LYM) in relation to tumor cell aneuploidy and proliferative state (S Fx). In Proc. of 17th Annual Mtg. of the American Society of Clinical Oncology, Vol. 22, P.520 April 1981.

Shackney, S.E., Schuette, W.H. and Lukes, R.J.:The Proliferative Behavior of Human Lymphomas. In Lymphomas Revisited: New Approaches to the Evaluation of Neoplastic Lymphoproliferative Disorders, (Lukes, R.J. and Parker, J.W., Editors) Churchill, Livingstone, New York (in press).

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10104-01

PERIOD COVERED

October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)

Isothermia

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	T. Talbot	Mechanical Engineer	ACES BEIB DRS
OTHER:	J. Ehrenkranz	Clinical Associate	NICHD DEB

COOPERATING UNITS (if any)

NICHD

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Applied Clinical Engineering

INSTITUTE AND LOCATION

DRS/NIH, Bethesda, Md. 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
0.5	0.4	0.1

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

The secretion of thyrotropin (TSH) from the human pituitary is characterized by a 2-5 fold increase in TSH concentration in blood during the early morning, corresponding to the time of fall in body temperature. This variation in TSH occurs without corresponding changes in T_3 and T_4, the hormones which serve as the main factors in the classical feedback regulation of TSH secretion. It also appears to be not related to the onset or stage of sleep. Somatostatin infusion given in the early morning as well as pharmacologic doses of glucocortoids will decrease serum TSH concentrations in normal individuals, but it is not yet clear whether these hormones play any role in TSH regulation under physiologic circumstances.

Z01 RS 10104-01 BEI

Objective: Prevent the night-time fall in core body temperature to investigate the corresponding effect of the nocturnal TSH peak.

Methods Employed: A synthetic thermoregulatory system has been constructed. A core body thermometer is placed on the anterior chest wall. This is connected via the GPIB to the Tektronix 4052. The computer reads the core temperature and adjusts a heating suit as required to maintain a core temperature to .1^{o}C of a preset level. Appropriate safety precautions are included.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10105-01

PERIOD COVERED

October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)

Adaptation of an EPICS II Flow Cytometer for T. Cruzi Analysis

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI: T.E. Hall — ACES, BEIB, DRS
J.S. Dvorak — LPD NIAID

COOPERATING UNITS (if any)

LPD-NIAID

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Applied Clinical Engineering

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, Md. 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
.8	.7	.1

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

An EPICS II Flow Cytometer is being used to perform cytometric analysis on a unicellular protozoan known as trypanosoma cruzi, the causative agent of Chagas disease. The EPICS II is composed of a fluid flow system for hydrodynamic focusing, a laser for excitation, signal processing electronics for data acquisition and a computer for data analysis. Developmental work is being carried out upon this system in order to improve the quality of the data acquired and the way in which it is analyzed. This includes modification of the various sensing systems to increase signal to noise ratio and the interfacing of a graphic display system in order to expand the data processing capability.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10106-01 BEI

PERIOD COVERED
October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)
Study of Fluorescein and Dextran Uptake in Tumors Using Chronic, Implanted Fiber Optic Probes

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	R.L.Levin	Mechanical Engineer	BEIB DRS
	R.L.Dedrick	Chief	ChES BEIB DRS
	P.M.Gullino	Chief	LPP NCI

COOPERATING UNITS (if any)
LPP-NCI

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Mechanical Engineering

INSTITUTE AND LOCATION
DRS, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
4.5	0.8	3.6

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Using an in vivo micro-fluorimetry system previously developed, we have employed carboxy fluorescein and fluorescently-tagged dextran tracers in an attempt to characterize the mass transport characteristics of solid tumors.

Objectives: To monitor the mass transport characteristics of solid tumors in order to facilitate the development of optimum drug modalities.

Significance: In growing tumors, the distribution of chemotherapeutic agents varies widely as a result of angiogenesis and necrosis. A quantitative understanding of mass transport in tumors is therefore essential for the development of optimum drug modalities. Unfortunately, common assay techniques requiring the dissection of tumors tend to mask these dynamic changes by yielding spatial distributions of marker substances at only a single instance of time. To facilitate the study of the transport properties of solid tumors under dynamic conditions, two new techniques have recently been developed. These techniques permit the direct in vivo long term monitoring of the concentration time course of fluorescently-tagged substances. This study involves the use of one of these techniques, namely, the in vivo microfluorimetry method previously developed in the laboratory, to monitor the transient mass transfer characteristics of solid tumors.

Major Findings and Proposed Course: Our results indicate that the transport of low molecular weight carboxy fluorescein is not "flow-limited" and that the transport of dextrans of molecular weights ranging from 20,000 to 150,000 daltons is not "membrane-limited." We are currently in the process of developing suitable transport models which will not only adequately describe our experimental findings but will also be capable of yielding values for the perfusion rate Q and the vascular permeability coefficient K.

Publications:

Levin, R. L., et al.: "A Microfluorimetry Study of Tumor Transport Characteristics", Adv. in Bioengineering, 1981 (In press).

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10107-01 BEI

PERIOD COVERED
October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)
Osmotic Behavior of Epithelial Cells

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	R.L.Levin	Mechanical Engineer	BEIB DRS
OTHER:	K.R.Spring	Senior Investigator	LKEM NHLBI
	J.L.Stephenson	Senior Investigator	DIR NHLBI

COOPERATING UNITS (if any)
LKEM-DIR-NHLBI

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Mechanical Engineering

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
0.05		

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Although water and ion transport by epithelia has been extensively studied during the last 25 years, several key pieces of information have yet to be obtained or are still in question. This includes accurate values for the passive (or possibly active) rate of water transport through epithelia, accurate values for the rate of passive and active ion transport through epithelia, and the precise manner in which epithelia regulate their size and the composition of their intracellular solution. The purpose of the present study is therefore to analyze the osmotic behavior of isolated epithelial cells.

Purposes: (1) To analytically characterize the osmotic behavior of epithelial cells. (2) To deduce from experimental observations of the osmotic responses of epithelial cells to changes in the composition of their suspending solutions, membrane(s) permeabilities of water and various ions.

Methods Employed: Mathematical modeling will be accomplished through the use of NIH's DEC-10 computing system.

Significance: The transport of water and ions across membrances is one of the basic ways in which cells maintain their normal biological activity. Study of the epithelial ion and water fluxes will therefore greatly enhance our knowledge about a fundamental life-sustaining activity.

Proposed Course: To continue the theoretical and experimental work already being conducted by Dr. K. Spring and associates of the Kidney and Electrolyte Branch of NHLBI.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10108-01 BEI

PERIOD COVERED
October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)
Thermodynamic Behavior of Cells and Tissues at Subzero Temperatures

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI: R.L.Levin Mechanical Engineer BEIB DRS

COOPERATING UNITS (if any)

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Mechanical Engineering

INSTITUTE AND LOCATION
DRS, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
0.06		

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

During the past twenty years, numerous models have been proposed to describe the osmotic behavior of biological cells during freezing and thawing. Although these studies have pinpointed the important biophysical parameters governing the volumetric response of cells at subzero temperatures they all have one serious drawback. Namely, all of the current models deal with a single, isolated cell suspended in an infinite amount of bathing solution which is being cooled or warmed uniformly at a constant rate. No provision is made for those common situations where (1) the volume of cells is comparable to the volume of the suspending solution or (2) the cellular system is cooled or warmed in a non-uniform manner with time due to the inability of the freeze-thaw device to handle the large amount of latent heat generated during freezing or adsorbed during thawing. The purpose of the present study is therefore to analytically investigate cellular osmotic behavior under non-ideal, but typical, freeze-thaw conditions.

Objectives: To analytically characterize the behavior of biomaterials during freezing and thawing in order to facilitate progress in attempts to successfully freeze-preserve cells, tissues and organs.

Methods Employed: Mathematical modeling will be accomplished through the use of NIH's DEC-10 computing system and associated computer graphics facilities.

Significance: Cryopreserving biological materials such as blood, sperm and ova, skin, and various other types of cells and tissues in research institutions and hospitals is a matter of great practical convenience since extremely low temperatures curtail metabolism and degenerative biochemical reactions. In fact, most biomaterials could probably be stored for milenia in a cryogenic environment. Unfortunately, in order to achieve this goal, cellular survival must be ensured during the critical cooling and warming periods associated with this form of storage. Consequently, further progress in the successful cryopreservation of cells, tissues, and organs necessitates an increased understanding of both the physical chemical events and the cellular responses that occur during a freeze-thaw cycle.

Major Findings: Our results indicate that the cytocrit of the cell suspension (Volume Cells/Total Volume Suspension) begins to significantly affect cellular volumetric behavior at levels above 10%. This is especially true for pre-frozen cell suspensions which are being warmed at very high rates in which case the cells are exposed to strongly hypotonic conditions just after the complete melting of the extracellular ice. Our results also indicate that most of the cellular water loss during freezing or gain during thawing may occur during the long temperature-time plateaus which usually occur just after the initial formation of extracellular ice during cooling and just before the final melting of the extracellular ice during warming rather than at lower or high temperatures.

Publications:

Levin, R.L.: "The Heterogeneous Freezing and Thawing of Aqueous Solutions." Trans. ASME. (In press).

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10109-01 BEI

PERIOD COVERED
October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)
Adjunct Heat Treatment of Cervical Cancer

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	R.L.Levin	Mechanical Engineer	BEIB DRS
	E.J.Glatstein	Chief	ROB NCI

COOPERATING UNITS (if any)
ROB-NCI.

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Mechanical Engineering

INSTITUTE AND LOCATION
DRS, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
0.02		

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

The purpose of this project is to facilitate the development of adjunct hyperthermia treatments of cervical cancer by theoretically and experimentally studying the spatial and temporal variation in the temperature field of tissues subjected to microwave EM radiation.

Objectives: (1) To develop a generalized mathematical model which will predict the spatial and temporal variation of the temperature field within a tissue of organ subjected to microwave irradiation. (2) To measure the spatial and temporal variation of the temperature field in the cervical area of humans undergoing therapy. (3) To facilitate the development of optimal adjunct hyperthermia modalities.

Methods Employed: The mathematical modeling will be accomplished through the use of NIH's DEC-10 computing system and associated computer graphics facility. The experimental measurement of the temperature field within tissues subjected to microwave radiation will be accomplished through the use of a newly available electromagnetically insensitive fiber optic temperature probe.

Significance: At present the heat treatment of carcinogenic cells when combined with conventional radiotherapy and chemotherapy shows considerable promise in the management of cancer. Nevertheless, there still remain numerous important problems that must be resolved. Of paramount importance is the problem of generating and controlling uniform temperature fields within tissues. This study will therefore attempt to facilitate the development of optimum hyperthermia modalities by theroretically and experimentally studying the temperature fields within tissues subjected microwave EM radiation.

Proposed Course: To begin the development of a suitable mathematical model utilizing the "bioheat" transfer equation. To interface the temperature measurement study with the clinical trials of the Radiation Oncology Branch of NCI.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10110-01

PERIOD COVERED

October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)

Design of a Dual-3 Dimensional Position Monitor for Speech Analysis

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	E.C. Walker	Mechanical Engineer	BEIB, DRS
OTHER:	C.L. Ludlow	Lab of Comm. Disorders	NINCDS
	M. Dorn-Quine		

COOPERATING UNITS (if any)

NINCDS

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Applied Clinical Engineering

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, Md. 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
1.5	1.25	.25

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

An instrument to monitor facial movements during articulation has been designed. The device consists of two, mirror image, transducers mounted on a common head frame. Each transducer, which can be individually adjusted, is capable of measuring the movement of a point in three orthogonal planes. The primary use of this instrument will be to study the lip movement of both normal and abnormal subjects.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10111-01

PERIOD COVERED

October 1, 1980 to September 30, 1981

TITLE OF PROJECT (80 characters or less)

Analytical High Voltage Electron Microscopy and Mirage Analysis

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	C.C. Gibson	Electronics Engineer	BEIB, DRS
OTHER:	R.D. Leapman	Physicist	BEIB, DRS
	C.E. Fiori	Physical Scientist	BEIB, DRS
	K.E. Gorlen	Electronics Engineer	CSL, DCRT
	L.K. Barden		CSL, DCRT
	J.S. Delpriore		CSL, DCRT
	C.R. Swyt	Physicist	BEIB, DRS

COOPERATING UNITS (if any)

Computer Systems Laboratory, DCRT

LAB/BRANCH

Biomedical Engineering and Instrumentation

SECTION

Electrical and Electronic Engineering Section

INSTITUTE AND LOCATION

DRS, NIH, Bethesda, Md. 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
4.5	4.0	0.5

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

The computer interface for the 200 KeV Hitachi 7000 Electron Microscope is approximately 80% complete. When complete, the computer will be able to control the microscope to acquire bright field images, dark field images, x-ray images, and electron energy loss images, simultaneously as well as directly, being able to measure the beam current. The computer-microscope combination will also be able to acquire energy dispersive x-ray spectra and electron energy loss spectra. Energy selective elemental imaging will also be done.

Objectives: To provide a computer controlled 200 KeV analytical electron microscope suitable for studying biological samples using energy dispersive x-rays and electron energy loss.

Methods Employed: Major modifications have been made to the microscope to enable it to be controlled by the computer. We have also redesigned the spectrometer electronics to provide 60Hz AC field connection, faster pulse counting circuitry, an alignment circuit, and a remote magnet control.

Significance: The computer controlled acquisition system will allow the data to be collected more rapidly, therefore minimizing the radiation damage to the specimen. The other modifications have improved the resolution for energy loss by a factor of five and the count rates by 10^4.

Proposed Course: Complete the interface circuiting and add 120Hz AC field connection, Descanning circuits for the beam, and a Faraday cup to measure beam current.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10112-01

PERIOD COVERED

October 1, 1980 through September 30, 1981

TITLE OF PROJECT (80 characters or less)

Analysis of Microcirculation by Coherent Light Scattering

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	R.L. Bowman	Chief, Lab. Tech. Dev.	LTD NHLBI
	P.D. Bowen	Biologist	LTD NHLBI
	R. Bonner	Physicist	BEI DRS
OTHER:	R. Nossal	Physicist	PSL DCRT
	A. Tahmoush	Clinical Associate	NB NINCDS

COOPERATING UNITS (if any)

Biomedical Engineering and Instrumentation Branch, DRS

LAB/BRANCH

Laboratory of Technical Development

SECTION

NHLBI

INSTITUTE AND LOCATION

NIH, Bethesda, Md. 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
3	2	1

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

The purpose of this project is the development of a clinical, non-invasive monitor of tissue blood flow by analysis of the spectrum of Doppler scattered laser light. The NIH Laser Doppler Blood Flow Monitor has been demonstrated to be highly portable and clinically convenient with the new flexible 4m fiber optic probes and photodiode detection system. The probes withstand sterilization procedures and mechanical insult well and are suitable for operating room patient study. The linearity of the flow analysis processor has been demonstrated in a variety of tissues and clearly resolves physiologic flow changes including instantaneous pulsatile flow in the microcirculation. Muscle blood flow in over 50 patients with neuromuscular disease has been studied and preliminary data suggest that post occlusive reactive hyperemia responses may be primary or secondary indicators of disease state. Studies of scleroderma patients' skin blood flow have shown markedly reduced flows in advanced scleroderma with very high flows at telangiectasia. Clinical applications being developed for the instrument are: allergy testing - quantitative methodology, periocular blood flow as indicator of external-internal carotid artery flow and implied flow to circle of Willis.

Objectives: Ongoing clinical applications include muscle blood flow at open muscle biopsy in muscular dystrophy patients, skin blood flow in normals and scleroderma patients and potential for therapy assessment, skin blood flow in periocular and facial regions of patients with carotid artery occlusive disease as potential alternative to angiography, and allergy testing using quantitative skin flow responses. Specific objective at this stage is the application of the instrument and technique in the above variety of clinical and experimental problems.

Methods Employed: The present form of the apparatus has demonstrated its clinical convenience and portability.

Major Findings: (1) The fiber optic probe system greatly improved the convenience of remote and flexible attachment to the patient; (2) The mean frequency detection used to analyze the Doppler shifted light signal has proved to be the optimum analysis method for diffuse tissue scattering. We developed a rigorous theory which substantiates the validity of our analysis method. Empirically output flow levels in a given tissue as well as between tissues correlate well with alternative measures of flow cited in literature. Our output corresponds to 1 volt = 15 ml/min/100g tissue. Interacting with other researchers we have demonstrated the correctness of our processor algorithm and are actively communicating with commercial developers to insure that the proper analysis scheme is employed in the commercial version of this instrument; (3) Studies of human tissue blood flow have been conducted under several protocols at the Clinical Center and other locations. In addition to measurements of skin blood in clinical center patients and normals, we have made extensive measurements of human muscle blood flow in over 50 patients during open muscle biopsy. Resting flows and post occlusive reactive hyperemia were monitored. Preliminary data analysis suggest that there are flow levels and responses which may be primary or secondary indicators of the various muscle "organ" disease state. We have made measurements of clinical center patients and normals in the periorbital region of facial skin and have found differences in flow and response to carotid occlusion for the patients not found in normals. Our experiments indicated abnormal zygomaticorbital skin flow in one patient whose retinal arteries were becoming occluded with clots. Our goal was to be able to infer external carotid and internal carotid artery blood flow and implied flow to the circle of Willis and brain. Studies of blood flow and local contractility of epicardium and endocardium of the dog heart have shown that the complex wave form obtained in beating heart muscle can be analyzed as to separate contractile and flow curves by averaging over several cardiac cycles and subtracting a no-flow, contraction only signal from the combined signal.

Proposed Course: (1) Continue development of the instrument in collaboration with LTD and industry; (2) Cooperate in clinical trials to establish the instrument as a useful clinical and experimental tool.

Significance: The NIH Laser Doppler Blood Flow Monitor is an instrument which holds promise for study of the local tissue microcirculation. It has potential applications in the research laboratory, and in the clinical study of vascular disease, peripheral vascular disease, allergy-skin flow testing, screening of vaso-active drugs, and the monitoring of patients with unstable circulatory systems.

ublications:

Bonner, R.F.,Bowen, P.D., Clem, T.R., Nossal, R.: Laser Doppler Continuous Real Time Monitor of Pulsatile and Mean Blood Flow in Tissue Microcirculation Scattering Techniques Applied to Supramolecular Non-equilibrium Systems, Plenum press, 1981, p. 279-316.

Bonner, R.F. , Nossal, R.: A Model for Laser Doppler Measurements of Blood Flow in Tissue, Applied Optics, 20: 2097-2108, 1981.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 RS 10113-01 BEI

PERIOD COVERED
October 1, 1980 to September 30, 1981.

TITLE OF PROJECT (80 characters or less)

Nuclear Magnetic Resonance Imaging System for Infants

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	D. I. Hoult	Visiting Scientist	BEIB DRS
OTHER:	C.-N. Chen	Visiting Fellow	BEIB DRS
	F. Romeo	Guest Worker	BEIB DRS
	M. S. Silver	Electronics Engineer	BEIB DRS

COOPERATING UNITS (if any)
NICHD

LAB/BRANCH
Biomedical Engineering and Instrumentation

SECTION
Nuclear Magnetic Resonance Imaging

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, MD 20205

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
3.5	4.0	

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

One interesting and potentially extremely valuable application of NMR in medical diagnosis is the generation of two- or three-dimensional images within living subjects. Clear images of the distribution of water in biological objects, including humans, have been obtained with image reconstructions methods.

The system being developed within BEIB utilizes a novel spherical electromagnet completed as part of an earlier project and described in an earlier report. The NMR signals will be produced and processed by a novel pulse Fourier transform method, rotating frame zeugmatography. The major goal of our approach is to produce images of high quality in time intervals that are a fraction of the time required by other methods.

Objectives: The purpose of this project is to develop an NMR resonance imaging or zeugmatography system to be used for exploring applications of NMR to medical imaging. The size of the device will permit examination of babies with the primary goal of detecting fluid filled lesions.

Methods Employed:

Field Homogeneity

The magnetic field is being analyzed in spherical harmonics. The effects of dipoles and metal strips and rings on various orders of the field are being computed and verified experimentally. Homogeneity of 3 - 5 ppm can now be obtained in a volume of 18cm in diameter.

Contrast Optimization

The theoretical approach calls for establishing an optimum pulse sequence by maximizing the change in signal-to-noise ratio with respect to change in relaxation time so that a good contrast in relaxation times can be obtained in the image.

Flux Stabilizer was built to stabilize the magnetic field. Short time stability is better than we can measure - about 1 part in 10^7.

Array Processor

An Analogic Array Processor has been installed. Hardware and software are being modified to perform part of the calculations during the time of data collection. Collection of the data (1024 complex values), base line correction, followed by FT and display are now being performed in 25 msec.

Display System

A software package has been installed in large measure. The standard software is being modified in order to comply with the upgraded display hardware.

Computing

The core memory of the PDP 11/34 is being expanded to 256 KB. An extended memory monitory has been generated. A virtual memory device handler will be installed. All tests dealing with the method of computation have been done and the RT11 operating system has been patched where it was found to be deficient.

RF Probe

A large RF probe made from copper tubing has been constructed. It is tuned to 5MHz, the Q factor of the transmitting coils being about 600, while that of the receiver is about 900. The transmitting coils are capable of producing the requisite RF field with gradients established in the laboratory frame.

Proposed Course: The pulse programmer will be constructed. The display system will be expanded so as to accept 12 bits of digitized data. The entire system will be integrated with the PDP 11/34. Experiments in producing two dimensional images will be carried out on suitable phantoms.